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1. **The Dieckmann Condensation** - John P. Schaefer and Jordan J. Bloomfield
2. **The Knoevenagel Condensation** - G. Jones

CHAPTER 1

THE DIECKMANN CONDENSATION

(Including the Thorpe-Ziegler Condensation)

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CONTENTS

	PAGE
INTRODUCTION	3
MECHANISM	4
SCOPE AND LIMITATIONS	7
Four-Membered Rings	7
Five- and Six-Membered Rings	9
Seven-Membered and Larger Rings	10
Cyclizations Leading to Heterocyclic Systems	11
Intermolecular Ester Condensations Followed by Cyclization	12
Michael Condensations Followed by Cyclization	14
Direction of Ring Closure	16
Alkylation and the Reverse Dieckmann Condensation	21
Competition with the Acyloin Condensation	24
Failures in the Dieckmann Condensation	26
THE THORPE-ZIEGLER CONDENSATION	28
RELATED REACTIONS	30
OTHER METHODS OF PREPARING CYCLIC KETONES	32
Table I. Comparison of Methods for Preparing Cyclic Ketones	36
EXPERIMENTAL CONSIDERATIONS	37
EXPERIMENTAL PROCEDURES	40
Oil-Free Sodium Hydride	41
2-Carboxycyclopentanone	42
Cycloheptanone	42

1-Methyl-3-carbethoxy-4-piperidone Hydrochloride	42
3-Hydroxy-2,5-dicarbomethoxythiophene	43
2,5-Dimethyl-5-carbomethoxycyclopentanone	43
Diethyl 2-Methyl-3-oxo-1,4-cyclopentanedicarboxylate	44
<i>cis</i> -Bicyclo[5.2.0]nonan-4-one	44
2-Cyano-5-phenyleyclooct-1-enylamine	44

TABULAR SURVEY	45
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Table II. Condensations Leading to Carbocyclic Products	47
<i>A.</i> Condensations Leading to Four-Membered Rings	47
<i>B.</i> Condensations Leading to Five-Membered Rings	48
<i>C.</i> Condensations Leading to Six-Membered Rings	83
<i>D.</i> Condensations Leading to Seven-Membered Rings	114
<i>E.</i> Condensations Leading to Eight-Membered and Larger Rings	117

Table III. Dieckmann Condensations Leading to Heterocycles	122
<i>A.</i> Heterocycles Containing Oxygen	122
<i>B1.</i> Heterocycles Containing Sulfur in a Five-Membered Ring	123
<i>B2.</i> Heterocycles Containing Sulfur in a Six-Membered Ring	130
<i>B3.</i> Heterocycles Containing Sulfur in Seven-Membered and Larger Rings	133
<i>C1.</i> Heterocycles Containing Nitrogen in a Five-Membered Ring	134
<i>C2.</i> Heterocycles Containing Nitrogen in a Six-Membered Ring	143
<i>C3.</i> Heterocycles Containing Nitrogen in a Seven-Membered Ring	160
<i>C4.</i> Heterocycles Containing Nitrogen in an Eight-Membered Ring	163
<i>C5.</i> Heterocycles Containing Nitrogen in Nine-Membered and Larger Rings	166

Table IV. Intermolecular Ester Condensations Followed by Cyclization	168
<i>A.</i> Condensations Involving Two Different Esters and Leading to Carbo- cyclic Products	168
<i>B.</i> Condensations Involving Two Different Esters and Leading to Heterocyclic Products	173
<i>C.</i> Self-Condensations	176

Table V. Michael Condensations Followed by Cyclization	179
<i>A.</i> Reactions Leading to Carbocyclic Products	179
<i>B.</i> Reactions Leading to Oxygen Heterocycles	181
<i>C.</i> Reactions Leading to Sulfur Heterocycles	181
<i>D.</i> Reactions Leading to Nitrogen Heterocycles	183

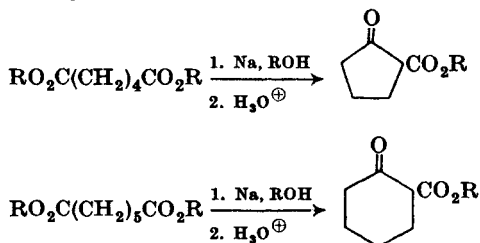
Table VI. Thorpe-Ziegler Condensations	186
<i>A.</i> Reactions Leading to Five-Membered Rings	186
<i>B.</i> Reactions Leading to Six-Membered Rings	188
<i>C.</i> Reactions Leading to Seven-Membered Rings	190
<i>D.</i> Reactions Leading to Eight- and Nine-Membered Rings	192
<i>E.</i> Reactions Leading to Ten-Membered and Larger Rings	193
<i>F.</i> Reactions Leading to Heterocycles Containing Nitrogen	194
<i>G.</i> Reactions Leading to Heterocycles Containing Oxygen	195
<i>H.</i> Reactions Leading to Heterocycles Containing Phosphorus or Arsenic	196

References for Tables II-VI	197
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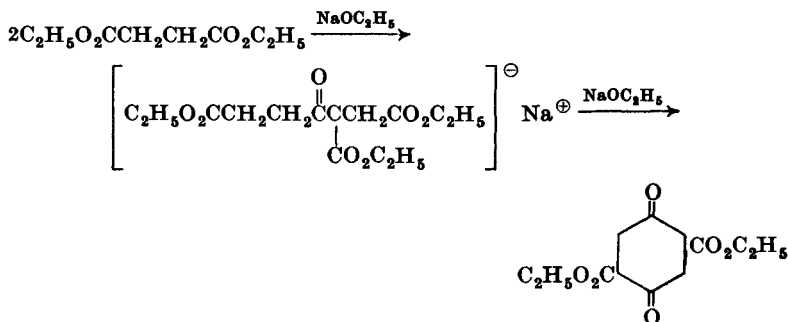
INTRODUCTION

The Dieckmann condensation is an acetoacetic ester condensation in which a dicarboxylic ester is cyclized to a β -ketonic ester* through the action of a base. The dicarboxylic ester must have at least one α -hydrogen atom and the carbalkoxy groups must be so situated that cyclization will result in a four-membered or larger ring.

Discovery and development of the reaction are generally credited to Dieckmann, who found that heating an adipic or a pimelic ester with sodium and a trace of alcohol led to cyclization with formation of a cyclopentanone or a cyclohexanone.¹



An earlier example of the reaction appears in the work of Fehling who, in the absence of adequate structural information, did not recognize and interpret the reaction correctly.² This example, the dimerization of diethyl succinate with sodium ethoxide, involves a Dieckmann condensation in the second stage.³⁻⁷



* The term β -ketonic ester is the editors' choice.

¹ Dieckmann, *Ber.*, **27**, 102 (1894).

² Fehling, *Ann.*, **49**, 192 (1844).

³ Herrmann, *Ann.*, **211**, 306 (1882).

⁴ Duisberg, *Ber.*, **16**, 133 (1883).

⁵ Baeyer and Noyes, *Ber.*, **22**, 2168 (1889).

⁶ Ebert, *Ann.*, **229**, 45 (1885).

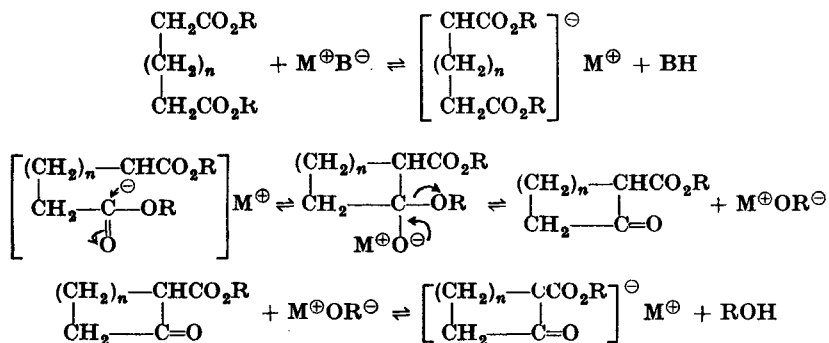
⁷ Herrmann, *Ber.*, **16**, 1411 (1883).

The Dieckmann condensation has proved useful for the preparation of a variety of carbocyclic and heterocyclic ketones and recently has been extended to the synthesis of seven- and eight-membered and larger rings. These developments have prompted the writing of this chapter in order to expand the brief survey given by Hauser and Hudson in their chapter on the acetoacetic ester condensation in Volume 1 of this series.⁸

A short review on the effect of substituents on the Dieckmann condensation has recently appeared.⁹ A review on the use of 2-carbethoxycyclopentanone in synthesis of more complicated molecules has also appeared.¹⁰ After submission of the first draft of this chapter, a comprehensive review was published by Russian workers.¹¹

MECHANISM

The general mechanistic considerations described by Hauser and Hudson also apply to the Dieckmann condensation and will not be repeated in detail. On the basis of the available data, the accompanying scheme describes the reaction path adequately. The initial step involves



rapid and reversible formation of the enolate ion of the ester. Recent studies suggest that, with metal alkoxides, it is the ion pair $\text{M}^\oplus\text{B}^\ominus$ which is the effective catalyst rather than the free base B^\ominus .¹²

Carriek and Fry have measured ¹⁴C isotope effects in the Dieckmann condensation.¹³ Their results show that the rate-determining step must

⁸ Hauser and Hudson, *Org. Reactions*, **1**, 266 (1942).

⁹ Chakravarti, *J. Proc. Inst. Chemists (India)*, **53**, 261 (1961); *Bull. Calcutta School Trop. Med.*, **9**, 157 (1961) [*C.A.*, **57**, 11009d (1962)].

¹⁰ (a) Mayer, *Angew. Chem.*, **53**, 169 (1956); (b) *Newer Methods of Preparative Organic Chemistry*, W. Foerst, ed., Academic Press, New York, 1963, pp. 101 ff.

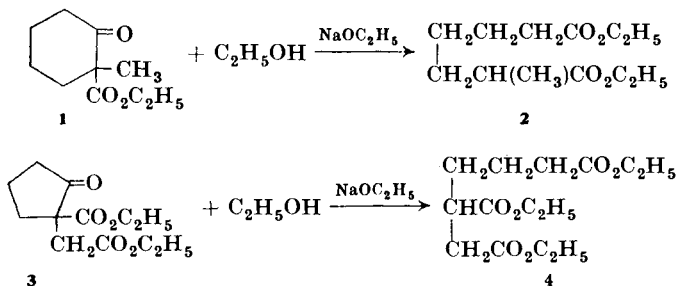
¹¹ Vul'fson and Zaretaki, *Reaktsii i Metody Issled. Organ. Soedin.*, **12**, 7 (1963) [*C.A.*, **59**, 7329a (1963)].

¹² Brändström, *Arkiv Kemi*, **11**, 527 (1967) [*C.A.*, **52**, 10049c (1958)].

¹³ Carriek and Fry, *J. Am. Chem. Soc.*, **77**, 4381 (1955).

be ring formation, i.e., attack of the ester function by the enolate ion. Rapid decomposition of the adduct through loss of alkoxide ion followed by formation of the enolate of the β -ketonic ester completes the reaction. The same conclusions had been reached earlier on the basis of kinetic studies on α - and β -substituted adipates.¹⁴

Each stage of the condensation must be completely reversible. This is demonstrated by the frequent utilization of the *reverse* Dieckmann condensation to convert cyclic β -ketonic esters to open-chain dicarboxylates.*¹⁵⁻²² A small amount of alkoxide in alcoholic solvent is sufficient to bring about the transformation, as the following examples for formation of a pimelic ester¹⁶ and an adipic ester²² show.†



The driving force in the Dieckmann condensation, as in other Claisen-type condensations, is provided by formation of the enolate of the β -ketonic ester. Condensation normally fails if this step is not possible. Again, the *reverse* Dieckmann condensation provides evidence for this requirement. Esters **1** and **3** cannot enolize; reversal of the condensation is facile. Under the proper conditions (one equivalent of alcohol-free base) the reversal is followed by ring closure in the other direction.

¹⁴ Reed and Thornley, *J. Chem. Soc.*, **1954**, 2148.

* References 15-22 are representative of some of the earliest examples. No attempt has been made to survey the *reverse* Dieckmann condensation, although many of the compounds listed in the tables were prepared in the course of syntheses leading to branched-chain adipic or pimelic esters.

¹⁵ Bouveault and Locquin, *Bull. Soc. Chim. France*, [4] **3**, 432 (1908).

¹⁶ Dieckmann, *Ann.*, **317**, 48 (1901).

¹⁷ Dieckmann, *Ann.*, **317**, 78 (1901).

¹⁸ Dieckmann, *Ann.*, **317**, 93 (1901).

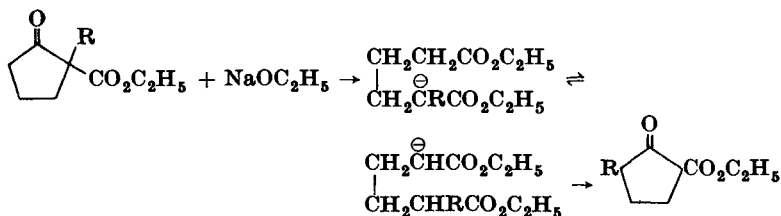
¹⁹ Kötz and Schöler, *Ann.*, **350**, 217 (1906).

²⁰ Kötz, *Ann.*, **357**, 192 (1907).

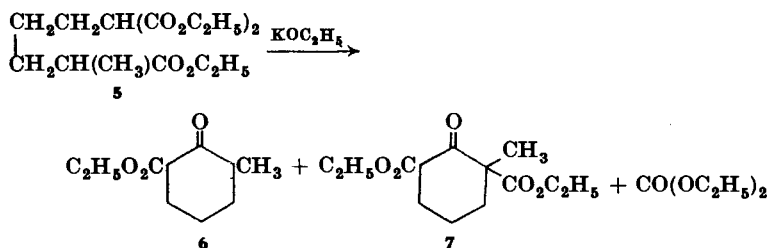
²¹ Kötz and Kayser, *Ann.*, **350**, 243 (1906).

²² Kötz, *Ann.*, **350**, 229 (1906).

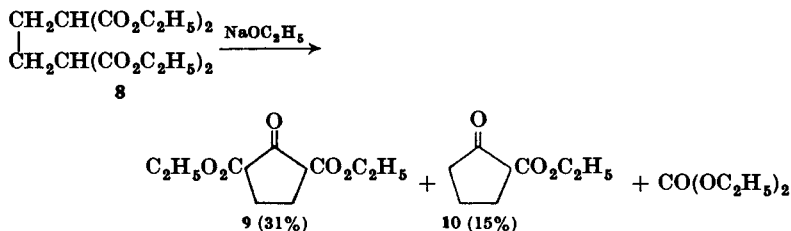
† In these and in subsequent reactions the intermediate enolate ions are not shown, unless necessary for clarity.



A reverse Claisen condensation of another kind, elimination of diethyl carbonate, enhances enolate stability and thus drives the equilibrium toward product in a number of condensations involving geminal dicarboxylic ester groups on one or more ends of the molecule.²³⁻³² This situation occurs in the conversion of the tricarboxylic ester, **5**, to a mixture of the mono- and di-carboxylic ester ketones, **6** and **7**.³¹



Diethyl α,α' -dicarbethoxyadipate (**8**), a tetracarboxylic ester, produces 2,5-dicarbethoxycyclopentanone (**9**) and 2-carbethoxycyclopentanone (**10**).²³



²³ Meineke, Cox, and McElvain, *J. Am. Chem. Soc.*, **57**, 1133 (1935).

²⁴ Kierstead, Linstead, and Weedon, *J. Chem. Soc.*, **1952**, 3610.

²⁵ Kierstead, Linstead, and Weedon, *J. Chem. Soc.*, **1952**, 3616.

²⁶ Guha and Hazra, *J. Indian Chem. Soc.*, **17**, 107 (1940).

²⁷ Guha and Seshadriengar, *Ber.*, **69**, 1212 (1936).

²⁸ Kon and Nandi, *J. Chem. Soc.*, **1933**, 1628.

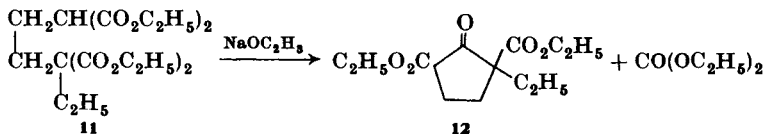
²⁹ Ushakov, *J. Russ. Phys. Chem. Soc.*, **61**, 795 (1929) [*C.A.*, **23**, 4678 (1929)].

³⁰ Nandi, *J. Indian Chem. Soc.*, **11**, 277 (1934).

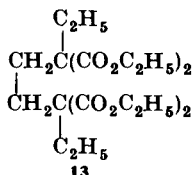
³¹ Zaretskii and Vul'fson, *Zh. Obshch. Khim.*, **31**, 484 (1961); *J. Gen. Chem. USSR (English Transl.)*, **31**, 442 (1961) [*C.A.*, **55**, 22171c (1961)].

³² Zaretskii and Vul'fson, *Zh. Obshch. Khim.*, **28**, 388 (1958); *J. Gen. Chem. USSR (English Transl.)*, **28**, 382 (1958) [*C.A.*, **52**, 13658e (1958)].

In some instances loss of diethyl carbonate must occur if an enolate is to form. For example, the ester **11** is converted to **12** in 74% yield with concomitant production of diethyl carbonate.²³



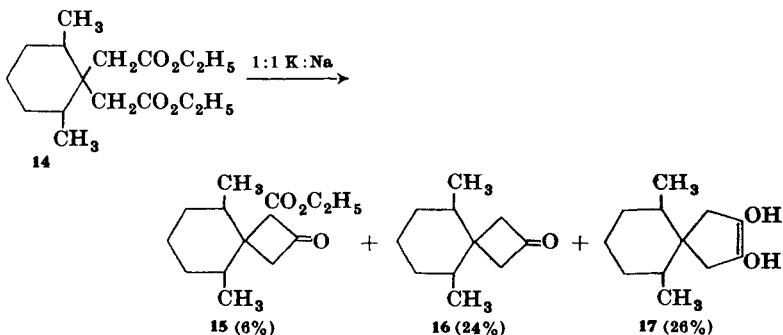
That the elimination of carbonate occurs after cyclization was demonstrated by the failure of ester **13** to cyclize even at 250°. All the other



decarbethoxylations occur easily under mild conditions ranging from the temperature of refluxing benzene solutions to 100°. A similar loss of diethyl carbonate, which occurs as a side reaction in alkylation of malonic esters, has been described in a previous volume of this series.³³

SCOPE AND LIMITATIONS

Four-Membered Rings. The Dieckmann condensation has been used to prepare cyclobutanones, but the yields have generally been so low that the method does not appear to be a practical route to these compounds. In only one instance, the conversion of diethyl 2,6-dimethylcyclohexane-1,1-diacetate (**14**) to the spirodecanones **15** and **16**,³⁴ has a yield of greater than 1% been reported. The acyloin **17** was also obtained in higher yield than either spirodecanone.



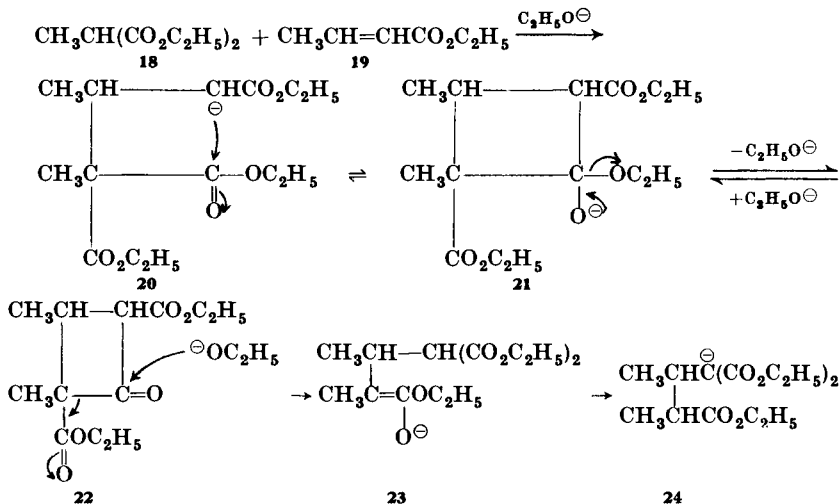
²³ Cope, Holmes, and House, *Org. Reactions*, **9**, 127-129 (1957).

³⁴ Varma, Maheshwari, and Bhattacharyya, *Tetrahedron*, **21**, 115 (1965).

It is probable that the increase in strain energy which accompanies the formation of a four-membered ring is sufficient to render the equilibrium unfavorable and is responsible for the low yields obtained. It should be possible to improve the yield by removing the alcohol as it is formed in order to shift the equilibrium toward product.

The loss of the carbethoxy group, as in 16, is frequently observed in Dieckmann condensations. Except for the special cases mentioned in the previous section, no attempt appears to have been made to determine whether this loss is accompanied by diethyl carbonate formation or whether the decarboxylation occurs during the isolation of the product. Since in many instances the ketone is the desired product, any loss of the carbalkoxyl group during the reaction would go unnoticed because the crude ketonic ester is usually directly hydrolyzed and decarboxylated.

Cyclobutanones are very likely intermediates in the "abnormal" Michael reaction.³⁵ The sequence for the reaction between diethyl methylmalonate and ethyl crotonate is shown below.^{36,37} The formation



of an enolate such as 24 appears to provide the driving force in the "abnormal" Michael reaction. Labeling experiments with ¹⁴C have shown that there is no rearrangement in the reaction of diethyl malonate with ethyl crotonate.³⁸ The details of the mechanism are still not available. Studies of the kinetic isotope effect on the carbon atom of the migrating

³⁵ Bergmann, Ginsburg, and Pappo, *Org. Reactions*, **10**, 191-197 (1959).

³⁶ Samuel and Ginsburg, *J. Chem. Soc.*, **1955**, 1288.

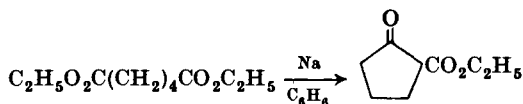
³⁷ Simamura, Inamoto, and Suehiro, *Bull. Chem. Soc. Japan*, **27**, 221 (1954) [*C.A.*, **49**, 7494e (1955)].

³⁸ Swan, *J. Chem. Soc.*, **1955**, 1039.

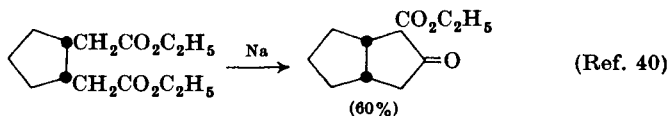
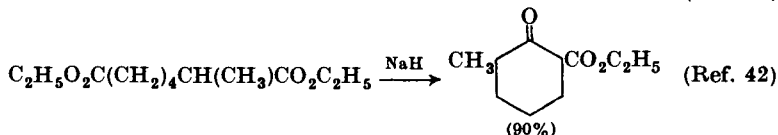
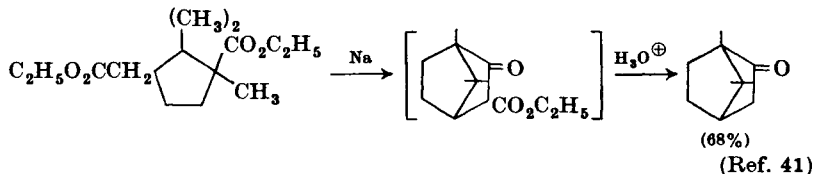
ester group and of the fate of labeled ethoxyl groups should enable one to decide whether **22** is an intermediate or the entire carboethoxyl group is transferred directly in proceeding from **21** to **23**.³⁹

Five- and Six-Membered Rings. The Dieckmann condensation is probably the best method of preparing cyclopentanones and cyclohexanones if the starting materials are available. The β -ketoic ester can serve as an intermediate for further reactions,¹⁰ or it can be directly decarboxylated.

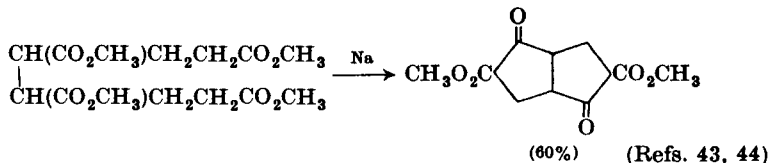
Conversions of up to 90% have been realized in the preparation of 2-carboethoxycyclopentanone.⁴⁰



Some other examples follow.



Two rings can be formed simultaneously as indicated in the following examples.



³⁹ Baker and Rothstein, *Chem. & Ind. (London)*, **1955**, 776.

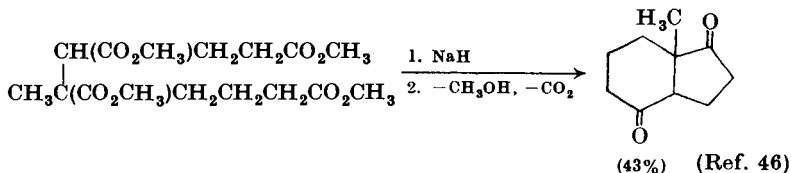
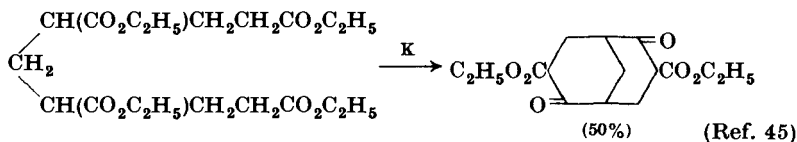
⁴⁰ Linstead and Meade, *J. Chem. Soc.*, **1934**, 935.

⁴¹ Ruzicka, *Helv. Chim. Acta*, **3**, 752 (1920).

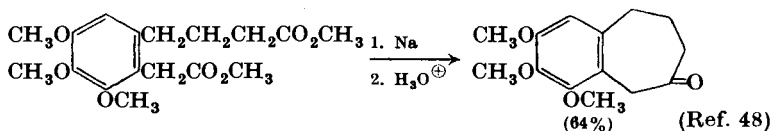
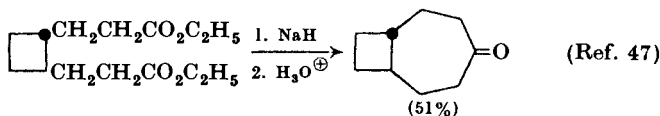
⁴² Banerjee and Mahapatra, *Tetrahedron*, **11**, 234 (1960).

⁴³ A. G. Osborne, Ph.D. Dissertation, University of Washington, March 1955 [*Dissertation Abstr.*, **16**, 240 (1956)].

⁴⁴ Blood and Linstead, *J. Chem. Soc.*, **1952**, 2255.



Seven-Membered and Larger Rings. Hydrolysis and decarboxylation of β -ketonic esters has provided an excellent path to seven-membered and larger ring ketones. Except for some of the seven-membered rings the cyclizations have usually been conducted under conditions of high dilution. The following examples illustrate the use of the reaction in the preparation of cycloheptanones.



Cyclooctanone itself is the only eight-membered ring carbocyclic ketone that has been prepared by Dieckmann cyclization.^{49,50} When the base is potassium *t*-butoxide, the dimeric diketone, 1,9-cyclohexadecanedione, is also formed.⁴⁹ Cyclizations of diethyl sebacate and diethyl 1,11-undecanedioate produce only the dimeric diketones, 1,10-cyclooctadecanedione and 1,11-cycloeicosanedione in yields of 11% and 12%, respectively.⁴⁹ Very low yields (0.5%) were obtained for the eleven- and twelve-membered cyclic ketones, but again fair yields of the dimeric diones were found.⁴⁹

⁴⁸ Stetter, Bänder, and Neuman, *Chem. Ber.*, **89**, 1922 (1956).

⁴⁹ Banerjee and Shafer, *J. Am. Chem. Soc.*, **72**, 1931 (1950).

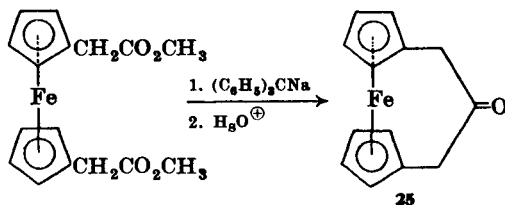
⁴⁷ Allinger, Nakazaki, and Zalkow, *J. Am. Chem. Soc.*, **81**, 4074 (1959).

⁴⁶ Rapoport and Campion, *J. Am. Chem. Soc.*, **73**, 2239 (1951).

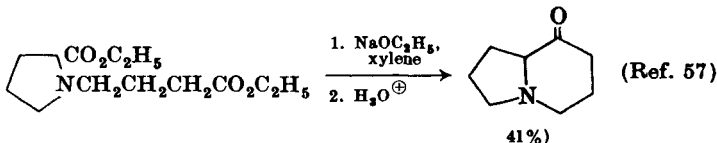
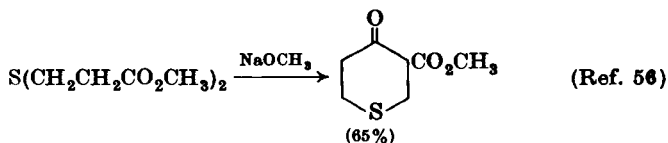
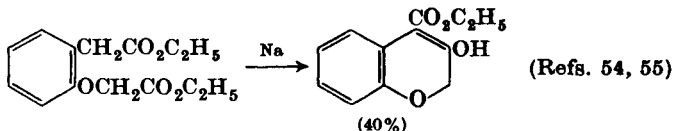
⁴⁵ Leonard and Schimelpfenig, *J. Org. Chem.*, **23**, 1708 (1958).

⁵⁰ Blicke, Azuara, Doorenbos, and Hotelling, *J. Am. Chem. Soc.*, **75**, 5418 (1953).

The dicarboxylic esters with twelve to fourteen methylene groups produced mixtures containing mostly monomeric ketones with smaller amounts of dimeric ketones.⁴⁹ Cyclophanes have also been prepared by the high-dilution Dieckmann cyclization.⁶¹ One particularly interesting example is the preparation of the ferrocenophanone⁵² **25** in 85% yield.⁵³



Cyclizations Leading to Heterocyclic Systems. The presence of a hetero atom in the ring-to-be, or elsewhere in the molecule, does not usually interfere with the course of cyclization. The following reactions typify the results obtained.



⁵¹ Schimelpfenig, Lin, and Waller, *J. Org. Chem.*, **28**, 805 (1963).

⁵² This nomenclature has been suggested by Smith, *Bridged Aromatic Compounds*, Academic Press, New York, 1964, pp. 8 ff.

⁵³ Mock and Richards, *J. Org. Chem.*, **27**, 4050 (1962).

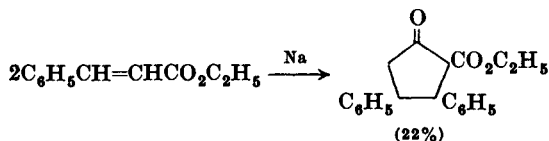
⁵⁴ Vul'fson and Podrezova, *Zh. Obshch. Khim.*, **32**, 3019 (1962); *J. Gen. Chem. USSR (English Transl.)*, **32**, 2968 (1962) [*C.A.*, **58**, 10159f (1963)].

⁵⁵ Hilton, O'Donnell, Reed, Robertson, and Rusby, *J. Chem. Soc.*, **1936**, 423.

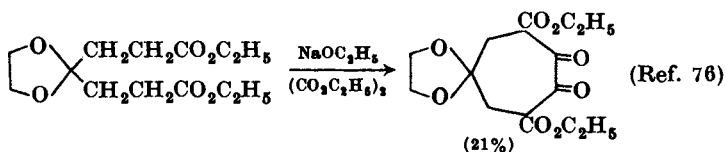
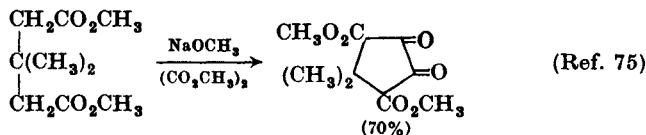
⁵⁶ Adlerova and Protiva, *Collection Czech. Chem. Commun.*, **24**, 1268 (1959).

⁵⁷ Leonard, Swann, and Figueras, *J. Am. Chem. Soc.*, **74**, 4620 (1952).

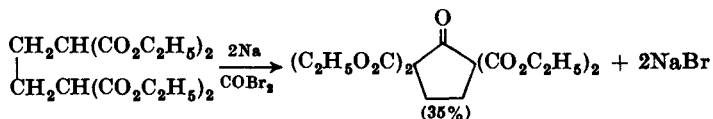
already been described.⁴⁹ Another example occurs in attempts to perform the acyloin reduction on cinnamic esters where bimolecular reduction precedes ring closure.⁶⁹⁻⁷²



The condensation of diethyl oxalate with other dicarboxylic esters, a reaction discovered by Dieckmann,⁷³ can lead to cyclopentanediones and in some cases to cycloheptanediones. However, the reaction fails with succinates and adipates.⁷⁴



A potentially interesting reaction involves the use of carbonyl bromide with 1,1,4,4-tetracarboxybutane.²⁷ In this case the loss of diethyl carbonate, discussed earlier, is avoided because a strongly basic alkoxide is not formed and the usual requirement of enolate formation is eliminated.



⁶⁹ Totton, Kilpatrick, Horton, and Blakeney, *J. Org. Chem.*, **30**, 1647 (1965).

⁷⁰ Totton, Freeman, Powell, and Yarboro, *J. Org. Chem.*, **26**, 343 (1961).

⁷¹ Bernhauer and Hoffman, *J. Prakt. Chem.*, **149**, 317 (1937).

⁷² Weidlich, *Ber.*, **71**, 1601 (1938).

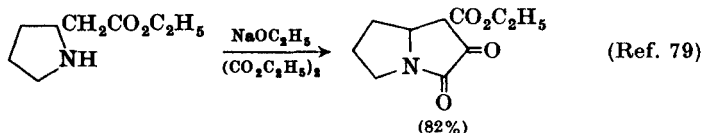
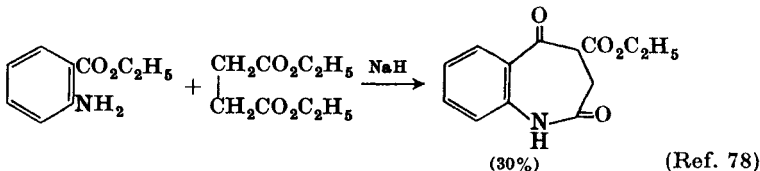
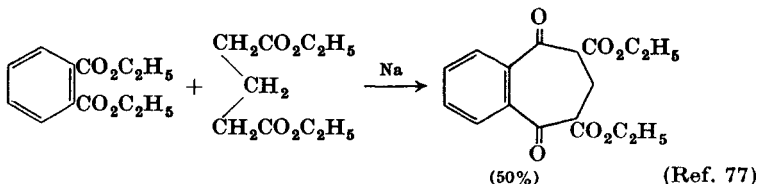
⁷³ Dieckmann, *Ber.*, **27**, 965 (1894).

⁷⁴ (a) Wislicenus and Nassauer, *Ann.*, **286**, 1 (1895); (b) Wislicenus and Schwanhäusser *Ann.*, **297**, 105 (1897).

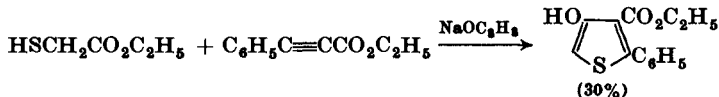
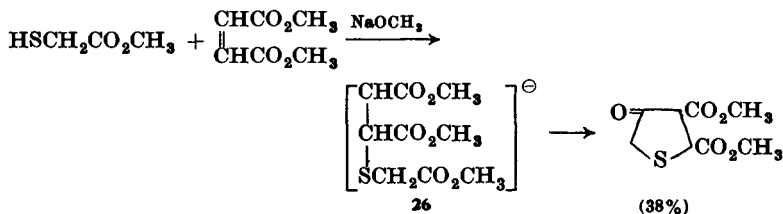
⁷⁵ Komppa, *Ann.*, **368**, 137 (1909).

⁷⁶ Gardner, Rand, and Haynes, *J. Am. Chem. Soc.*, **78**, 3425 (1956).

Other examples of the utility of bimolecular condensation are shown in the accompanying equations.



Michael Condensations Followed by Cyclization. The Michael condensation of methyl thioglycolate with dimethyl maleate leads to an intermediate anion **26**, which cyclizes to the Dieckmann product.⁸⁰ When acetylenic esters are used, the products are thiophene derivatives.⁸¹



These examples demonstrate a reaction sequence with considerable potential that has received only slight attention.

⁷⁷ Dieckmann, *Ber.*, **32**, 2227 (1899).

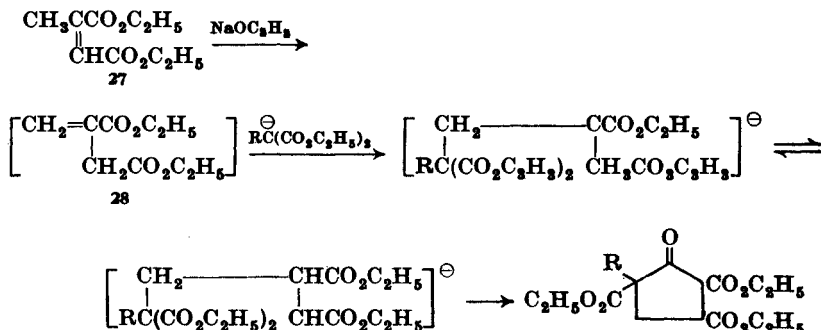
⁷⁸ MacPhillamy, Dziemian, Lucas, and Kuhne, *J. Am. Chem. Soc.*, **80**, 2172 (1958).

⁷⁹ Adams, Miyano, and Nair, *J. Am. Chem. Soc.*, **83**, 3323 (1961).

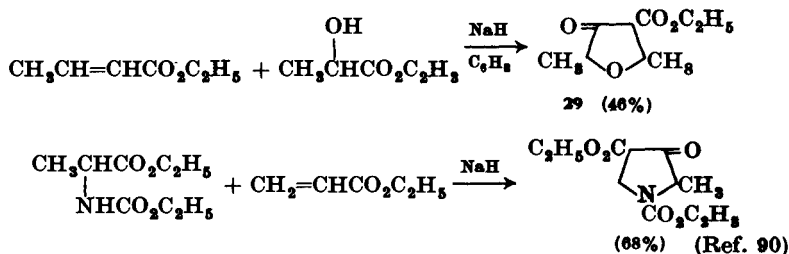
⁸⁰ Fiesaelmann and Schipprak, *Chem. Ber.*, **87**, 835 (1954).

⁸¹ Fiesaelmann, Schipprak, and Zeitler, *Chem. Ber.*, **87**, 841 (1954).

Unfortunately, the first examples of the reaction, recorded by Michael in 1900,⁸² are probably incorrect. The condensations of diethyl malonates with ethyl citraconate (**27**) in the presence of sodium ethoxide were reported to produce cyclobutanones. Later workers have shown that the products of condensations with ethyl citraconate in the presence of alkoxide are derived from the isomeric ethyl itaconate (**28**).⁸³⁻⁸⁶



Other examples of this version of the Dieckmann condensation include the preparation of the tetrahydrofuranone **29** from ethyl crotonate and ethyl lactate⁸⁷ and the synthesis of a variety of pyrrolidones.⁸⁸⁻⁹⁶



Only one example of the formation of a six-membered ring by means of this sequence has been reported. The condensation of two equivalents of

⁸² Michael, *Ber.*, **33**, 3731 (1900).

⁸³ See also Bergmann, Ginsburg, and Pappo, *Org. Reactions*, **10**, 236, 474 (1959). The formula on p. 474 does not correspond with the one in Michael's paper.⁸²

⁸⁴ Hope, *J. Chem. Soc.*, **101**, 892 (1912).

⁸⁵ Ingold, Shoppee, and Thorpe, *J. Chem. Soc.*, **1926**, 1477.

⁸⁶ Toivonen, John, Sainio, and Kuusinen, *Suomen Kemistilehti*, **33**, 46 (1935) [*C.A.*, **30**, 2185 (1936)].

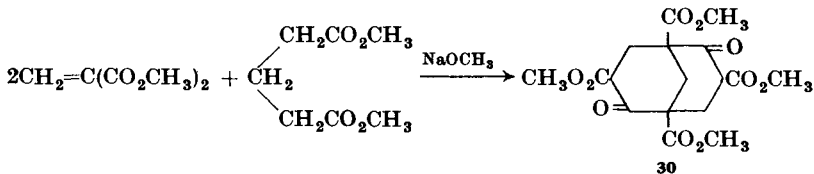
⁸⁷ J. J. Bloomfield and R. A. Martin, Unpublished work.

⁸⁸ Wu, Gould, Lobeck, Both, and Feldkamp, *J. Med. Pharm. Chem.*, **5**, 752 (1962).

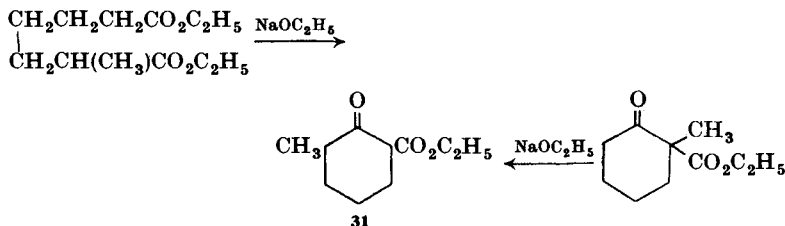
⁸⁹ Kuhn and Osswald, *Chem. Ber.*, **89**, 1423 (1956).

⁹⁰ Wu, Lobeck, and Feldkamp, *J. Med. Pharm. Chem.*, **5**, 762 (1962).

dimethyl methylenemalonate with dimethyl glutarate produces the bicyclononane derivative **30** in 66% yield.^{91, 92}



Direction of Ring Closure. In many instances ring formation can, in principle, lead to at least two different products. Only one of these will be produced if the other cannot form a stabilized enolate. This is the case in the preparation of 2-carbethoxy-6-methylcyclohexanone (**31**) from diethyl 2-methylpimelate. The isomeric 2-carbethoxy-2-methylcyclohexanone is, in fact, easily converted to **31** by sodium ethoxide.⁹³



The effect of substituents on carbon atoms adjacent to the potentially enolic center is important. It has been suggested that in β -substituted adipic or pimelic esters cyclization to the adjacent methylene group will not occur if the other possible product can be formed;^{10, 94, 95} i.e., the least hindered anion of both the original ester and of the product ketone is favored.

An example is the conversion of diethyl β -methyladipate to a mixture consisting of at least 80% 4-methyl-2-carbethoxycyclopentanone (**32**).⁹⁶ The condensation has been effected by sodium metal,^{17, 97-99} sodium

⁹¹ Meerwein, *J. Prakt. Chem.*, [2] **104**, 161 (1922).

⁹² Meerwein and Schürmann, *Ann.*, **398**, 196 (1913).

⁹³ Vul'fon and Zaretskii, *Zh. Obshch. Khim.*, **29**, 2737 (1959); *J. Gen. Chem. USSR (English Transl.)*, **29**, 2704 (1959) [*C.A.*, **54**, 10895c (1960)].

⁹⁴ Chakravarti, *Experientia*, **3**, 149 (1947) [*C.A.*, **42**, 2593e (1948)].

⁹⁵ Chakravarti, *J. Chem. Soc.*, **1947**, 1028.

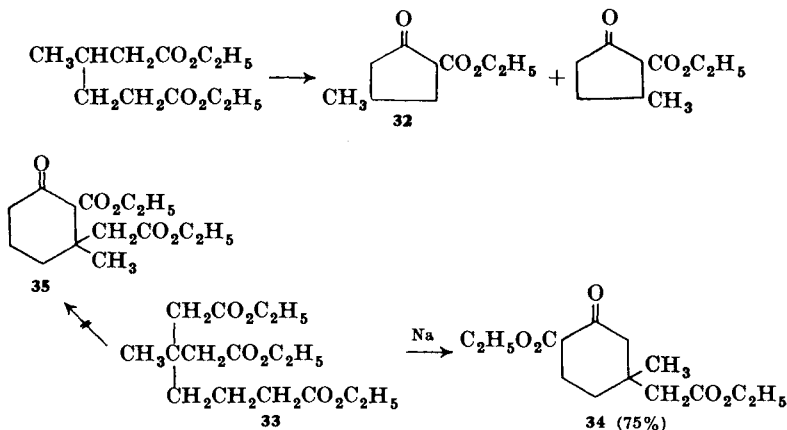
⁹⁶ Lochte and Pittman, *J. Org. Chem.*, **25**, 1462 (1960).

⁹⁷ Staudinger and Ruzicka, *Helv. Chim. Acta*, **7**, 245 (1924).

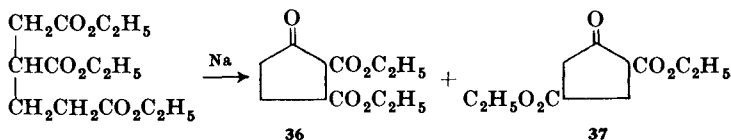
⁹⁸ Haller and Desfontaines, *Compt. Rend.*, **140**, 1205 (1905).

⁹⁹ Haller and Desfontaines, *Compt. Rend.*, **136**, 1613 (1903).

amide,¹⁰⁰ or sodium ethoxide.^{14, 96, 101} Similarly, cyclization of diethyl 3-methyl-3-carbethoxymethylpimelate (33) leads to the cyclohexanone 34, not the isomeric ketone 35.¹⁰²



When the β -substituent is an ester group the situation is reversed, and the favored product is the 2,3-dicarbethoxy derivative. In the simplest case, the cyclization of 1,2,4-tricarbethoxybutane,¹⁰³⁻¹⁰⁷ the ratio of the two products, 36 and 37, varies from 2.6:1 to 4.5:1 as the solvent is changed from diethyl ether to xylene.¹⁰⁵ Since the reactions were conducted at reflux, the change probably represents a shift in equilibrium brought about by the increase in temperature.



The effect of temperature on the direction of ring closure is illustrated in the cyclization of the unsymmetrical sulfide 38. The product can be

¹⁰⁰ Haller and Cornubert, *Compt. Rend.*, **158**, 1618 (1914).

¹⁰¹ Dieckmann and Groeneveld, *Ber.*, **33**, 595 (1900).

¹⁰² Farmer and Ross, *J. Chem. Soc.*, **127**, 2358 (1925).

¹⁰³ Toki, *Bull. Chem. Soc. Japan*, **32**, 233 (1959) [*C.A.*, **54**, 4416h (1960)].

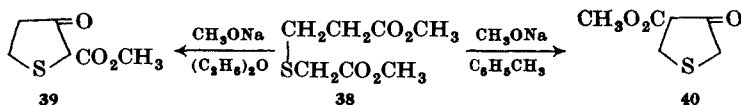
¹⁰⁴ Kay and Perkin, *J. Chem. Soc.*, **89**, 1640 (1906).

¹⁰⁵ Ruzicka, Borges de Almeida, and Brack, *Helv. Chim. Acta*, **17**, 183 (1934).

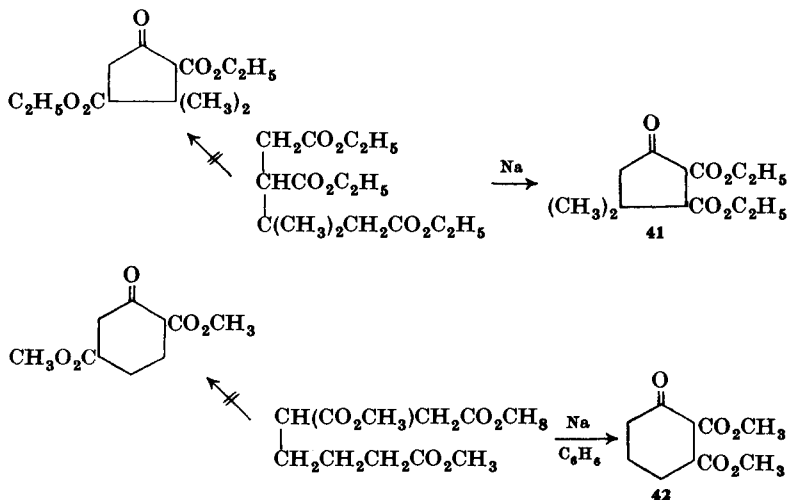
¹⁰⁶ Vul'fson and Zaretskii, *Zh. Obshch. Khim.*, **34**, 828 (1964) [*C.A.*, **60**, 15747d (1964)].

¹⁰⁷ Shemyakin, Shechukina, Vinogradova, Kolosov, Vdovina, Karapetyan, Rodionov, Ravdel, Shvetsov, Bamdas, Chaman, Ermolaev, and Semkin, *Zh. Obshch. Khim.*, **27**, 742 (1957); *J. Gen. Chem. USSR (English Transl.)*, **27**, 817 (1957) [*C.A.*, **52**, 17130a (1958)].

varied from mostly 2-carbomethoxy-3-thiophanone (**39**) to exclusively 4-carbomethoxy-3-thiophanone (**40**) by raising the temperature from the boiling point of diethyl ether to the boiling point of toluene.¹⁰⁸ The role of solvation in this case cannot be neglected, but neither can it be exactly specified.



Further examples of the effect of an ester group in the β position are the conversions of 3,3-dimethyl-1,2,4-tricarbethoxybutane¹⁰⁹ and 1,2,5-tricarbomethoxypentane¹¹⁰ to the 2,3-dicarbethoxy esters **41** and **42**, respectively.¹¹¹



When an ester and another group are both β -substituents the product is again the one derived from the least hindered enolate. The cyclization of 2-methyl-1,2,4-tricarbethoxybutane has been shown to produce chiefly the 4-methyl-4-carbethoxy derivative **43**,¹¹² and not the isomeric compound **44** as was earlier supposed.¹¹³

¹⁰⁸ Woodward and Eastman, *J. Am. Chem. Soc.*, **68**, 2229 (1946).

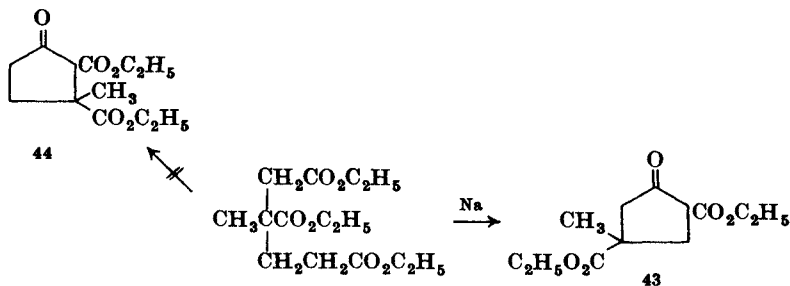
¹⁰⁹ Perkin and Thorpe, *J. Chem. Soc.*, **89**, 778 (1906).

¹¹⁰ M. J. D'Errico, Ph.D. Thesis, Columbia University [*Dissertation Abstr.*, **21**, 52 (1960)].

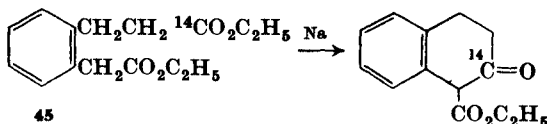
¹¹¹ See also the discussion by Chakravarti, *J. Chem. Soc.*, **1953**, 1315.

¹¹² Chakravarti, *J. Indian Chem. Soc.*, **20**, 173 (1943).

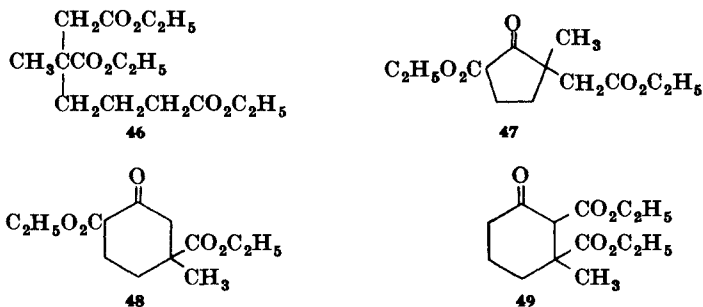
¹¹³ Baker, *J. Chem. Soc.*, **1931**, 1546.



Cyclization of the dicarboxylic ester **45**, labeled as indicated with ^{14}C , showed that the benzylic position is the more reactive one; on hydrolysis and decarboxylation no $^{14}\text{CO}_2$ was formed.¹¹⁴



Some esters present the possibility of cyclizing either to a five- or a six-membered ring. The examples cited above suggest that Dieckmann condensation of 2-methyl-1,2,5-tricarboethoxypentane (**46**) should produce the cyclopentanone **47** or the cyclohexanone **48**, but not the isomeric cyclohexanone **49**.⁹⁴ The cyclopentane derivative is the only cyclization product isolated,¹¹⁵⁻¹¹⁸ although the yield varies with the base used.¹¹⁸



The absence of any cyclohexanone has been explained in terms of a strong 1,3 diaxial interaction between the methyl group and an $-\text{O}^\ominus$ or

¹¹⁴ Stepanov, Iodko, and Vul'fson, *Ukr. Khim. Zh.*, **23**, 489 (1957) [*C.A.*, **52**, 6293c (1958)].

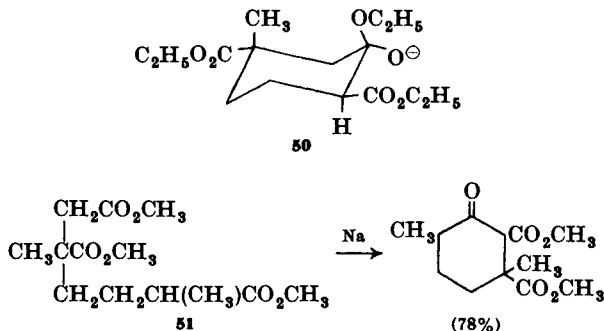
¹¹⁵ Goldberg, Hunziker, Billeter, and Rosenberg, *Helv. Chim. Acta*, **30**, 200 (1947).

¹¹⁶ Banerjee, *J. Indian Chem. Soc.*, **17**, 453 (1940).

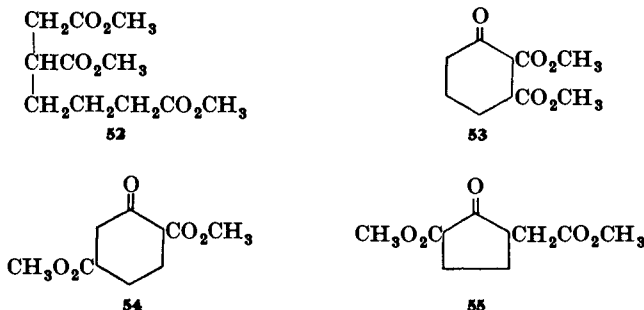
¹¹⁷ Chakravarty and Banerjee, *J. Indian Chem. Soc.*, **23**, 377 (1946).

¹¹⁸ Dutta and Biswas, *J. Indian Chem. Soc.*, **38**, 335 (1961).

—OC₂H₅ in the transition state **50**.¹¹⁸ A related argument involving a boat transition state in the cyclization of 2-methyl-1,2,5-tricarboethoxyhexane (**51**), has been used to account for the fact that ring closure is effected by sodium dust in benzene but not by sodium methoxide.¹¹⁹



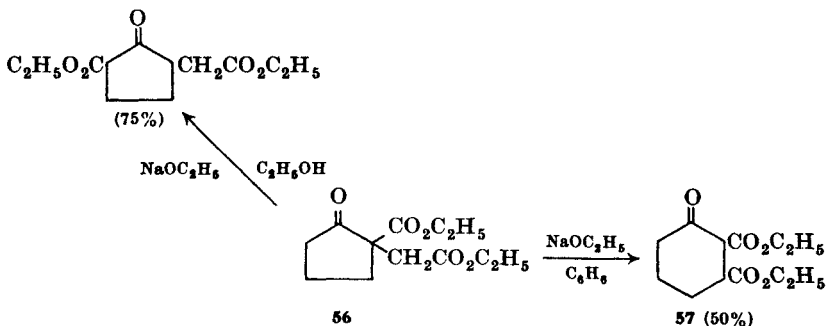
The direction of cyclization of 1,2,5-tricarboethoxypentane (**52**), a lower homolog of the ester **51** which is lacking the 2-methyl group, is influenced by the solvent. In benzene with sodium metal as base the ester **52** gives a mixture consisting of 81% of 2,3-dicarboethoxycyclohexanone (**53**) and 19% of the cyclopentanone **55**.¹¹⁰ However, when sodium methoxide is used as the base in methanol, the product is made up of 85% of the cyclopentanone **55** and 15% of a mixture of **53** and **54**.¹¹⁰ In benzene the cyclohexanone and the cyclopentanone are apparently formed as products of kinetic control, whereas in methanol the equilibrium product mixture is formed. Evidence for this view is provided by the



observation that ring opening and recyclization of 2-carboethoxy-2-carboethoxymethylcyclopentanone (**56**) with dry sodium ethoxide in

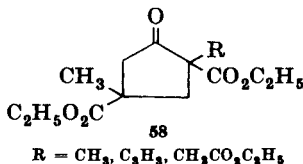
¹¹⁹ Dutta and Biswas, *J. Indian Chem. Soc.*, **38**, 385 (1961).

benzene leads to the cyclohexanone **57**, but in ethanol the product is the isomeric cyclopentanone.^{111, 120, 121}



Much more work is necessary before we can be sure that most of the factors affecting the direction of ring closure are even partially understood. Particular emphasis should be made of the need to determine accurately all the products of the cyclization as systematic changes are made in the structure of the starting ester, the base, the solvent, and the temperature at which the reaction is conducted.

Alkylation and the Reverse Dieckmann Condensation. When the β -ketonic ester is to be directly decarboxylated the question, "In which direction does the ring close?" becomes academic. Both members of each pair of products discussed in the preceding section (with the exception of the five-membered and six-membered ring isomers) lead to the same ketone on hydrolysis and decarboxylation. The need to know in which direction the ring closes becomes important when cyclization is to be followed by alkylation and other reactions. One example occurs in the cyclization of 2-methyl-1,2,4-tricarbethoxybutane to 4-methyl-2,4-dicarbethoxycyclopentanone (**43**) (equation on p. 19). Direct alkylation of the enolate of **43** with methyl iodide,¹¹² ethyl bromoacetate,¹²² or ethyl iodide¹²³ leads to a 2-alkyl-4-methyl-2,4-dicarbethoxycyclopentanone **58**.



¹²⁰ Chatterjee, Das, and Barpujari, *J. Indian Chem. Soc.*, **17**, 161 (1940).

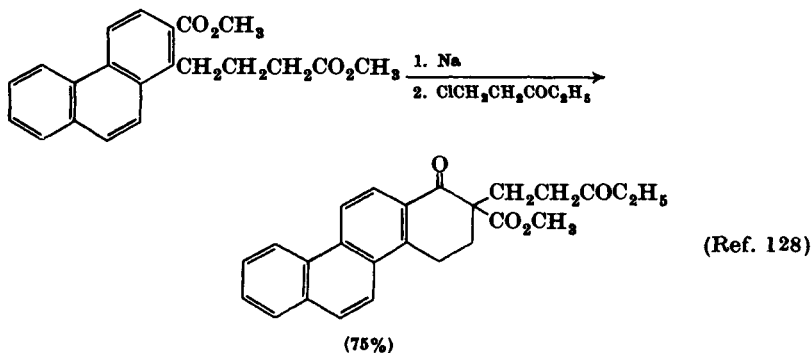
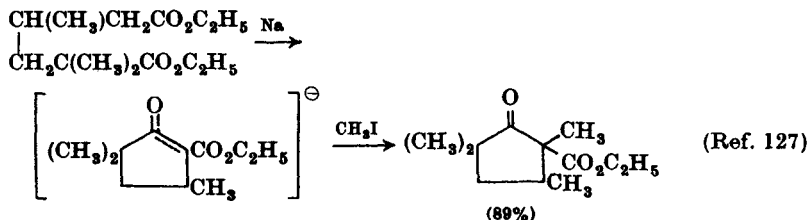
¹²¹ Banerjee, Dutta, and Bagavant, *Proc. Indian Acad. Sci.*, **46A**, 80 (1957) [*C.A.*, **52**, 3701b (1958)].

¹²² Chakravarti, *J. Indian Chem. Soc.*, **20**, 247 (1943).

¹²³ Chakravarti, *J. Indian Chem. Soc.*, **20**, 189 (1943).

Alkylation with ethyl β -chloropropionate leads to a product that should be formulated as **58**, $R = CH_2CH_2CO_2C_2H_5$.^{*} 122, 124, 125

Alkylation is usually accomplished by adding the alkyl halide directly to the enolate without isolating the Dieckmann product. Occasionally the Dieckmann product is isolated, converted to its enolate with sodium or sodium hydride in an aprotic solvent, and then alkylated. Although no attempt has been made to record examples of the second technique, the tables include many examples of the first procedure; the examples in the remainder of this section are typical, as are those described in the preceding paragraph.



Recently the preparation of 2,5-dimethyl-2-carbomethoxycyclopentanone (**59**) in 76% yield from dimethyl adipate without isolation of a single intermediate was described.¹²⁹ This technique should be compared

* The erroneous structure assigned to this alkylation product, together with reasons for the assignment, descriptions of the chemical transformations of the product, and the evidence for the revision of the structural assignment are given in references 122, 124, 125, and 126.

¹²⁴ Banerjee, *J. Indian Chem. Soc.*, **17**, 423 (1940).

¹²⁵ Banerjee, *Sci. Cult. (Calcutta)*, **5**, 566 (1940) [*C.A.*, **34**, 4363^a (1940)].

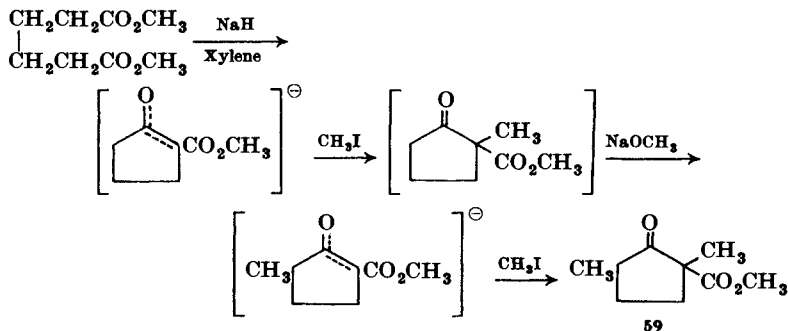
¹²⁶ Raha and Mukharji, *J. Org. Chem.*, **19**, 1376 (1954).

¹²⁷ Bardhan and Adhya, *J. Chem. Soc.*, **1956**, 2179.

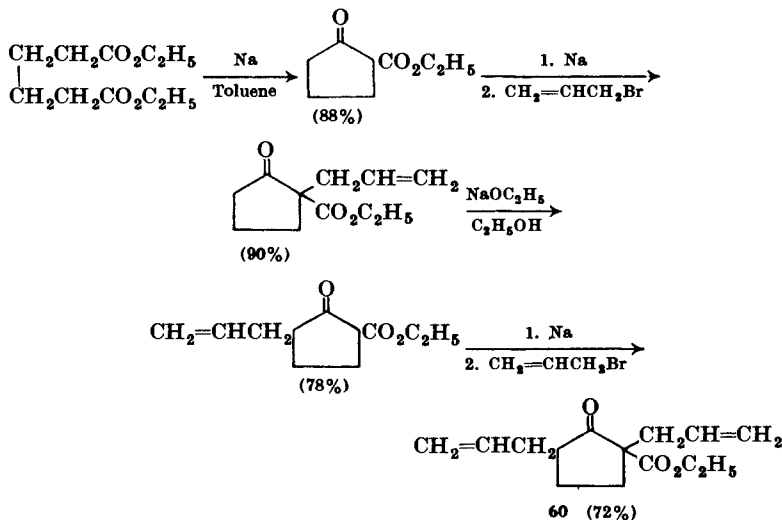
¹²⁸ Nasipuri and Roy, *J. Indian Chem. Soc.*, **36**, 817 (1959).

¹²⁹ Meyer, Lobo, and Marquis, *J. Org. Chem.*, **30**, 183 (1965). This synthesis is described in the section on Experimental Procedures.

with the much more tedious procedure that has been used until now, in which each intermediate has been isolated and purified before the next



step was undertaken. For example, the preparation of 2,5-diallyl-2-carbethoxycyclopentanone (**60**) was accomplished in an overall yield of only 44% from diethyl adipate; each intermediate was isolated.¹³⁰



Each of the examples shows the utilization of the reverse Dieckmann condensation, mentioned earlier,¹⁵⁻²² followed by immediate recyclization to the isomeric ketone. Procedures have been described for conducting the reverse Dieckmann in such a way as to provide either the open-chain dicarboxylic ester or the isomeric cyclic ketone.^{131, 132} Azeotropic distillation of the alcohol produced during the condensation raises the

¹³⁰ Marvel and Moyer, *J. Am. Chem. Soc.*, **79**, 4990 (1957).

¹³¹ Sisido, Utimoto, and Isida, *J. Org. Chem.*, **29**, 2781 (1964).

¹³² Nicole and Berlinguet, *Can. J. Chem.*, **40**, 353 (1962).

yield of cyclization product and decreases the amount of unchanged dicarboxylic ester.^{131, 133}

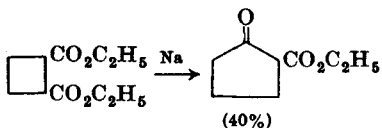
Competition with the Acyloin Condensation. In a few attempted cyclic acyloin condensations the product actually isolated is the result of a Dieckmann condensation. The basic conditions for the two reactions can be very similar, i.e., an alkali metal dispersed in an inert solvent. In the Dieckmann condensation a small amount of anhydrous alcohol is often added to initiate the reaction; thus the actual basic catalyst is probably the alkoxide. Despite the fact that alkoxide is generated in the acyloin condensation, Sheehan was able to convert diethyl adipate to adipoin in 55% yield by using four equivalents of sodium metal and a high-speed stirrer.¹³⁴ No 2-carbethoxycyclopentanone was present.

That the acyloin condensation occurs at all indicates that this reaction is normally fast compared to the competing Dieckmann condensation. Any factor that slows down the acyloin condensation or speeds up the Dieckmann condensation can alter the situation sufficiently to favor the Dieckmann product, and conversely. Because not many examples of Dieckmann intervention in acyloin condensations have been recorded, all those that have been found in the literature are included in this section.

The cyclization of diethyl 2,6-dimethyl-1,1-cyclohexanediacetate (14) by a large excess of a 1:1 alloy of sodium and potassium to a mixture of the cyclobutanones 15 and 16 and the acyloin 17 was described on p. 7. The fact that nearly equal amounts of acyloin and Dieckmann product were obtained suggests that the factors influencing the two reactions were nearly in balance.

The preparation of 3,4-diphenyl-2-carbethoxycyclopentanone from methyl cinnamate, described on p. 13, is the first reported instance of a Dieckmann condensation occurring under acyloin reaction conditions.⁷¹ The reaction involves a conjugate bimolecular reduction followed by cyclization.

An attempt to prepare the bicyclo[2.2.0]hexane system by acyloin condensation of 1,2-dicarbethoxycyclobutane also involves reduction and leads to 2-carbethoxycyclopentanone.¹³⁵

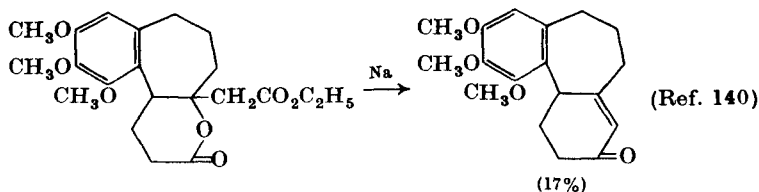
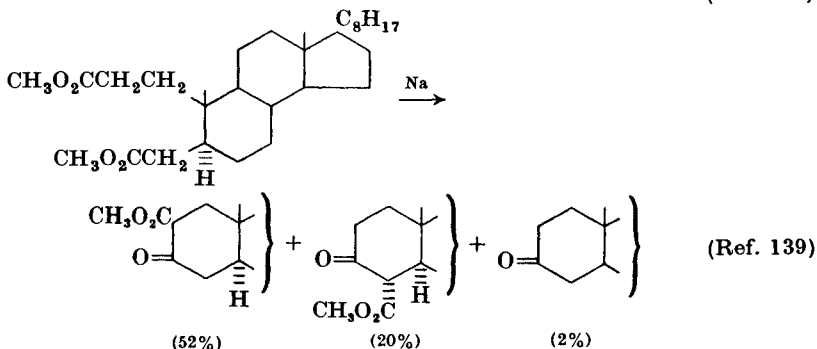
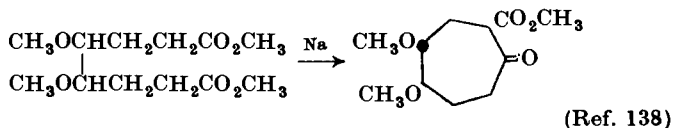
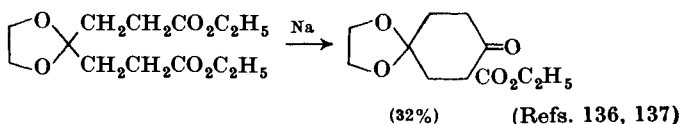
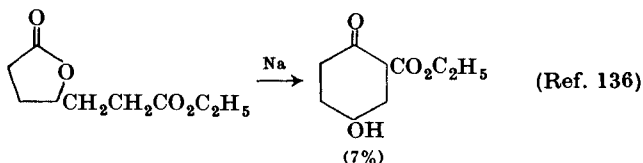
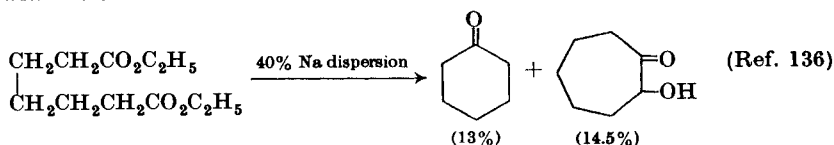


¹³³ Prill and McElvain, *J. Am. Chem. Soc.*, **55**, 1233 (1933). This synthesis is described in the section on Experimental Procedures.

¹³⁴ Sheehan, O'Neill, and White, *J. Am. Chem. Soc.*, **72**, 3376 (1950).

¹³⁵ Bloomfield, Todd, and Takahashi, *J. Org. Chem.*, **28**, 1474 (1963).

The following reactions have also been reported and are presented without comment.



¹³⁶ Gardner, Haynes, and Brandon, *J. Org. Chem.*, **22**, 1206 (1957).

¹³⁷ Leonard, Miller, and Berry, *J. Am. Chem. Soc.*, **79**, 1482 (1957).

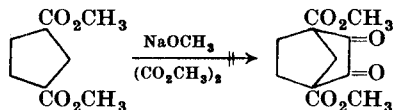
¹³⁸ Cope and Mehta, *J. Am. Chem. Soc.*, **86**, 1268 (1964).

¹³⁹ Nelson and Schut, *J. Am. Chem. Soc.*, **80**, 6630 (1958).

¹⁴⁰ van Tamelen, Spencer, Allen, and Orvis, *Tetrahedron*, **14**, 8 (1961).

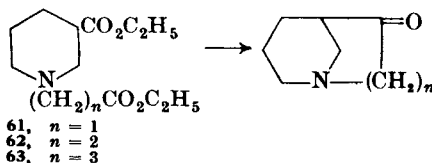
Phenyl esters are reported to be unreactive in the Dieckmann condensation.^{140a} This finding suggests that phenyl esters of some of the reactants described in this section should undergo normal acyloin condensation.

Failures in the Dieckmann Condensation. The Dieckmann condensation fails when a stable enolate of the product cannot be formed. For example, the failure of dimethyl 1,3-cyclopentanedicarboxylate to condense with dimethyl oxalate stems from such a difficulty.¹⁴¹ Few



examples have been reported; the realization that condensation will not occur usually prevents the attempt.

In some instances failure may be traced to a poor choice of base. Attempts to cyclize ethyl 3-carbethoxypiperidino-1-acetate (**61**), β -propionate (**62**), or γ -butyrate (**63**) by sodium ethoxide or sodium amide or by pyrolysis of the thorium salts all met with failure.¹⁴² However, the use of potassium ethoxide in toluene has produced 71% and 48% of the ketones derived from cyclization and decarboxylation of **61**¹⁴³ and



62,¹⁴⁴ respectively. Potassium metal has also been used successfully to cyclize **61** and **62**, but the yields are lower.¹⁴⁵ No other attempts have been made to cyclize **63**, but cyclization is to be expected under the proper conditions.

Attempted cyclization of indole derivatives has frequently met with failure. Examples are furnished by the esters **64** and **65** which have resisted cyclization under Dieckmann conditions.

^{140a} J. P. Schaefer and M. Moran, Unpublished results.

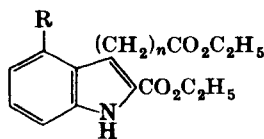
¹⁴¹ Guha and Ranganathan, *Ber.*, **69**, 1199 (1936).

¹⁴² Clemo, Ormston, and Ramage, *J. Chem. Soc.*, **1931**, 3185.

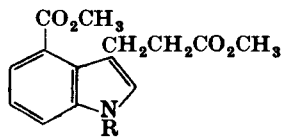
¹⁴³ Yanina and Rubtsov, *Zh. Obshch. Khim.*, **29**, 485 (1959); *J. Gen. Chem. USSR (English Transl.)*, **29**, 485 (1959) [*C.A.*, **53**, 21957e (1959)].

¹⁴⁴ Yanina and Rubtsov, *Zh. Obshch. Khim.*, **30**, 526 (1960); *J. Gen. Chem. USSR (English Transl.)*, **30**, 548 (1960) [*C.A.*, **54**, 24708g (1960)].

¹⁴⁵ Sternbach and Kaiser, *J. Am. Chem. Soc.*, **74**, 2215 (1952).

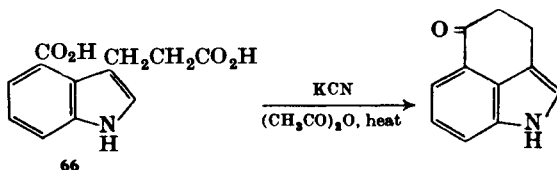


$R = H, n = 2$ (Ref. 146)
 $R = H, n = 3$ (Ref. 146)
 $R = CO_2C_2H_5, n = 2$ (Ref. 147)

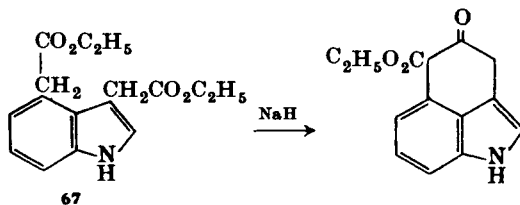


$R = H$ or CH_3CO (Ref. 148)

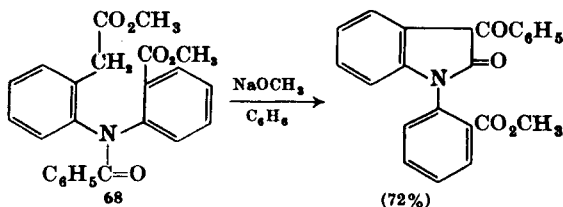
Pyrolysis of the acid **66** or its barium or calcium salt gave no ketone. Cyclization was finally effected by heating the free acid in boiling acetic anhydride containing a catalytic amount of potassium cyanide.¹⁴⁸



The difficulty of effecting this cyclization is made even more striking by the observation that diethyl indole-3,4-diacetate (**67**) is readily cyclized in 86% yield by sodium hydride.¹⁴⁹



Another interesting failure occurred in the attempt to cyclize the diphenylamine derivative **68** with sodium methoxide in benzene.¹⁵⁰ The product isolated arises from a rearrangement involving migration of the benzoyl group.



¹⁴⁸ Elks, Elliott, and Hems, *J. Chem. Soc.*, **1944**, 624.

¹⁴⁷ Koelsch, *J. Org. Chem.*, **8**, 295 (1943).

¹⁴⁶ Uhle, *J. Am. Chem. Soc.*, **71**, 761 (1949).

¹⁴⁹ Plieninger and Müller, *Chem. Ber.*, **93**, 2029 (1960).

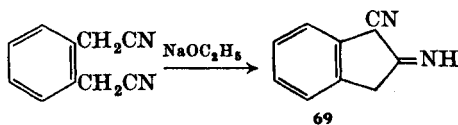
¹⁵⁰ Schulenberg and Archer, *J. Am. Chem. Soc.*, **83**, 3091 (1961).

It is probable that esters that have so far resisted attempts at cyclization will cyclize when the proper choice of base and reaction conditions is made.

THE THORPE-ZIEGLER CONDENSATION

The Thorpe-Ziegler condensation (the cyclization of dinitriles to enamionitriles) has been included in this chapter because of its similarity to the Dieckmann condensation. It has been especially valuable in the synthesis of medium- and large-ring compounds.

The intermolecular dimerization of nitriles had been previously studied¹⁵¹⁻¹⁵³ by Thorpe and his co-workers when, in 1908, Moore and Thorpe described the first example of the cyclization of a dinitrile.¹⁵⁴ A catalytic amount of sodium ethoxide was used as the base; the product **69** was characterized as the imine, and strong arguments were presented in favor of this structure.



Until recently the products of all nitrile cyclization reactions had been formulated as imines. In 1955 Hammer and Hines¹⁵⁵ pointed out that the product from adiponitrile was better described as an enamine. Since 1955 the enamine structure for the cyclization product of dinitriles has been confirmed for other five-membered,¹⁵⁶⁻¹⁵⁸ six-membered,^{159, 160} seven-membered,¹⁵⁹ and eight-membered¹⁶¹ rings. Baldwin¹⁵⁹ has examined the infrared and ultraviolet spectra of acyclic and five-, six-, and seven-membered ring enamionitriles. In all these compounds the band for —CN is at abnormally low frequencies (between 2165 and 2190 cm^{-1} in all the cyclic compounds). The ultraviolet spectra of simple enamionitriles (unsubstituted amino nitrogen) all have λ_{max} 258–265 $\text{m}\mu$ with ϵ_{max}

¹⁵¹ Baron, Remfry, and Thorpe, *J. Chem. Soc.*, **85**, 1726 (1904).

¹⁵² Atkinson and Thorpe, *J. Chem. Soc.*, **89**, 1906 (1906).

¹⁵³ Atkinson, Ingham, and Thorpe, *J. Chem. Soc.*, **91**, 578 (1907).

¹⁵⁴ Moore and Thorpe, *J. Chem. Soc.*, **98**, 165 (1908).

¹⁵⁵ Hammer and Hines, *J. Am. Chem. Soc.*, **77**, 3649 (1955).

¹⁵⁶ Thompson, *J. Am. Chem. Soc.*, **80**, 5483 (1958).

¹⁵⁷ Bloomfield and Fennessey, *Tetrahedron Letters*, **1964**, 2273.

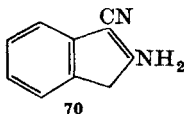
¹⁵⁸ House, Wickham, and Müller, *J. Am. Chem. Soc.*, **84**, 3139 (1962).

¹⁵⁹ Baldwin, *J. Org. Chem.*, **28**, 3288 (1961).

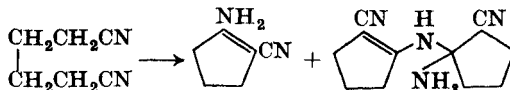
¹⁶⁰ Baldwin, *J. Org. Chem.*, **28**, 3280 (1961).

¹⁶¹ Cope and Cotter, *J. Org. Chem.*, **29**, 3467 (1964). The synthesis described in this paper is presented in the section on Experimental Procedures.

about 14,000. Similar observations have been recorded for the eight-membered ring.¹⁶¹ Nuclear magnetic resonance chemical shift and integration data have been used to show that there is an —NH_2 rather than an =NH present in five-membered¹⁵⁷ and eight-membered rings.¹⁶¹ This evidence suggests that compound **69** is also an enamine and should be formulated as **70**; unless proved otherwise, dinitrile cyclization products should be considered to be enamines.



Thorpe used trace amounts of sodium ethoxide in the three cyclizations he described.^{154, 162, 163} Thompson found, however, that adiponitrile did not cyclize with small amounts of ethoxide.¹⁵⁶ With an equivalent of ethoxide, a Michael dimer was obtained as well as the expected product. A trace of sodium *t*-butoxide in *t*-butyl alcohol produced mostly the dimer, 67–76%, while an equivalent of this base in toluene gave the monomer in 85% yield.



The cyclization of diethyl α, α' -dicyanoadipate is of historical interest. The reaction was first conducted by Carpenter and Perkin in 1899, but they suggested an incorrect structure for the product.¹⁶⁴ Ten years later Best and Thorpe established the correct structure in one of their early papers on the cyclization of dinitriles.¹⁶³

In a series of papers, beginning in 1933, Ziegler and his co-workers showed that, after modification, Thorpe's reaction could be applied to the synthesis of cyclic ketones containing from seven to thirty-three carbon atoms.^{165–170} The modifications involved: (a) conducting the reaction under high-dilution conditions, a technique developed by Ziegler, to avoid the bimolecular reactions that lead to dimers and polymers; (b) using diethyl ether as the solvent; and (c) using an amide as the base. In

¹⁶³ Thorpe, *J. Chem. Soc.*, **95**, 1901 (1909).

¹⁶⁴ Best and Thorpe, *J. Chem. Soc.*, **95**, 685 (1909).

¹⁶⁵ Carpenter and Perkin, *J. Chem. Soc.*, **75**, 921 (1899).

¹⁶⁶ Ziegler, Eberle, and Ohlinger, *Ann.*, **504**, 94 (1933).

¹⁶⁷ Ziegler and Lüttringhaus, *Ann.*, **511**, 1 (1934).

¹⁶⁸ Ziegler and Weber, *Ann.*, **512**, 164 (1934).

¹⁶⁹ Ziegler and Aurnhammer, *Ann.*, **513**, 43 (1934).

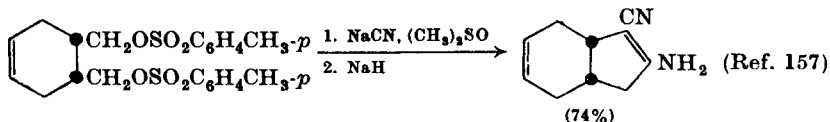
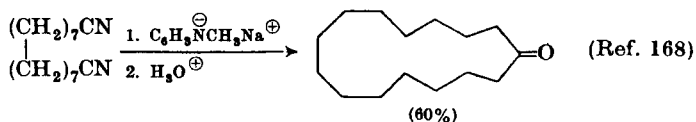
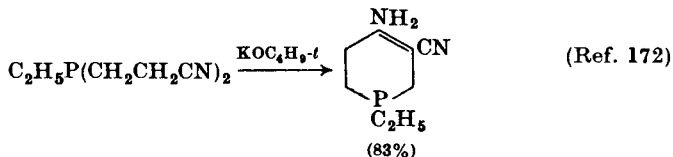
¹⁷⁰ Ziegler and Hechelhammer, *Ann.*, **528**, 114 (1937).

¹⁷¹ Ziegler and Holl, *Ann.*, **528**, 143 (1937).

the first work lithium ethyl anilide or lithium diethyl amide was used.¹⁶⁵ In later publications sodium alkyl anilide was described as the base of preference; the alkyl group was not specified. In a review of the methods available for the synthesis of large-ring compounds Ziegler notes that sodium methyl anilide is the preferred base and that the lithium derivative is not so effective.¹⁷¹

Despite its obvious utility, especially in the synthesis of large rings, the Thorpe-Ziegler reaction has received relatively little attention. In part, this may stem from the unavailability of the necessary dinitriles. In the synthesis of five- and six-membered rings the difficulty with which the enamionitrile is hydrolyzed and decarboxylated may militate against this method and favor the Dieckmann condensation. The problems in hydrolysis have been discussed by Baldwin and useful hydrolysis techniques described.¹⁶⁰ The Dieckmann product appears to be a more versatile intermediate; it can be alkylated, readily converted to an acyclic ester, and recycled. No such reactions of Thorpe-Ziegler intermediates have been described.

The following examples present a cross section of the reactions listed in Table VI.



RELATED REACTIONS

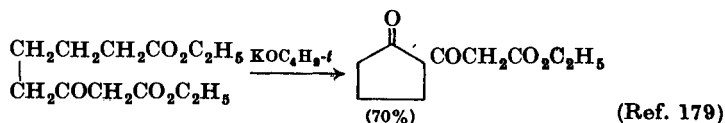
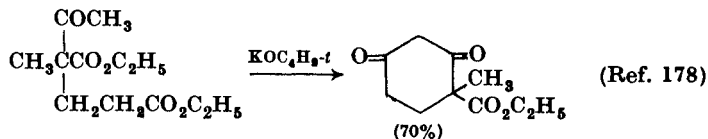
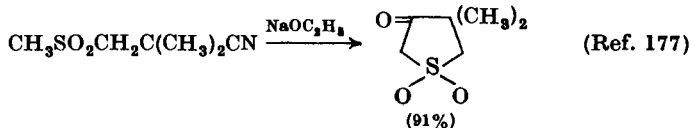
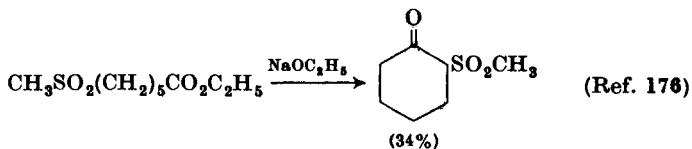
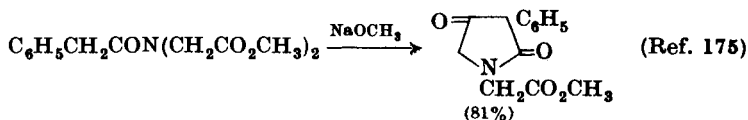
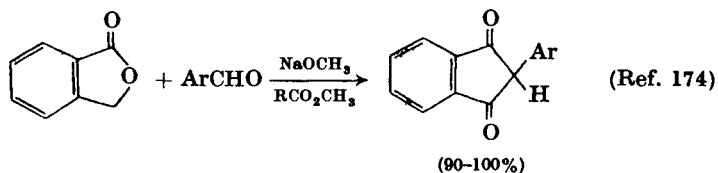
There are a number of reactions which, like the Dieckmann and Thorpe-Ziegler condensations, are internal Claisen condensations. The reaction conditions are often identical with those used for the Dieckmann, but the products are not β -ketonic esters or their Thorpe analogs. Such

¹⁷¹ K. Ziegler in *Methoden der Organischen Chemie* (Houben-Weyl) *Allgemeine Chemische Methoden*, Band IV, Teil 2, Georg Thieme Verlag, Stuttgart, 1955, pp. 729 ff.

¹⁷² Welcher, Johnson, and Wystrach, *J. Am. Chem. Soc.*, **82**, 4437 (1960).

reactions may be described as "occurring under Dieckmann conditions" but should not be called Dieckmann condensations.

One example, the cyclization of γ -, δ -, ϵ -, and ζ -ketonic esters which leads to cyclic β -diketones, has been described in Volume 8 of *Organic Reactions*.¹⁷³ The accompanying condensations include some other interesting examples of reactions similar to the Dieckmann or Thorpe-Ziegler condensations.



¹⁷³ Hauser, Swamer, and Adams, *Org. Reactions*, **8**, 79 (1954).

¹⁷⁴ (a) Shapiro, Geiger, and Freedman, *J. Org. Chem.*, **25**, 1860 (1960); (b) Shapiro, Geiger, Youlus, and Freedman, *J. Org. Chem.*, **26**, 3580 (1961).

¹⁷⁵ Koelsch and Robinson, *J. Org. Chem.*, **21**, 1211 (1955).

¹⁷⁶ Truce and Knospe, *J. Am. Chem. Soc.*, **77**, 5063 (1955).

¹⁷⁷ Truce, Bannister, and Knospe, *J. Org. Chem.*, **27**, 2821 (1962).

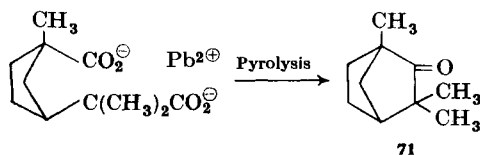
¹⁷⁸ Mukherji, Sharma, and Vig, *J. Chem. Soc.*, 1958, 4770.

¹⁷⁹ Allan and Sneed, *Tetrahedron*, **18**, 821 (1962).

OTHER METHODS OF PREPARING CYCLIC KETONES*

The principal use of both the Dieckmann and Thorpe-Ziegler condensations is in the synthesis of cyclic ketones, which are prepared by hydrolysis and decarboxylation of the initial condensation products. For five- and six-membered rings the overall yield is seldom higher with other methods. Occasionally one of the methods described below is better. For nine-through fourteen-membered rings, for example, the acyloin condensation is probably the best method.

The pyrolysis of salts of dicarboxylic acids was used as early as 1879 as a method for preparing cyclic ketones.¹⁸⁰ In the late 1920's Ruzicka and his co-workers published the first of a series of papers on the pyrolysis of cerium, thorium, and yttrium salts of dicarboxylic acids.¹⁸¹⁻¹⁸⁷ Ruzicka had already used the pyrolysis of lead salts in his proof of the structure of fenchone (71).¹⁸⁸ This is one example of a reaction for which the Dieckmann condensation cannot be used.



Pyrolysis gives fair yields for five- and six-membered rings. For the synthesis of C₉-C₁₃ ketones the yields are about 0.5%. The yield rises to a maximum of about 5% at C₁₈ as the series is ascended and then gradually decreases. The cyclic ketones are contaminated with ketones of lower molecular weight, with acyclic ketones, and even with small quantities of dimeric diketones. Despite the drawbacks of low yield and

* Several of the methods described in this section have been particularly useful in the synthesis of large-ring compounds. The review of Ziegler¹⁷¹ has already been mentioned. Raphael, in Rodd, ed., *Chemistry of Carbon Compounds*, Vol. II-A, Elsevier Publishing Company, New York, 1953, pp. 270 ff., also describes much of the same material. Smith, *Bridged Aromatic Compounds*, Academic Press, New York, 1964, has described a variety of methods for the synthesis of large rings with particular reference to cyclophanes.

¹⁸⁰ Dale and Schorlemmer, *Ann.*, **199**, 144 (1879).

¹⁸¹ Ruzicka, Stoll, and Schinz, *Helv. Chim. Acta*, **9**, 249 (1926).

¹⁸² Ruzicka and Brugger, *Helv. Chim. Acta*, **9**, 339 (1926).

¹⁸³ Ruzicka and Brugger, *Helv. Chim. Acta*, **9**, 389 (1926).

¹⁸⁴ (a) Ruzicka, Brugger, Seidel, and Schinz, *Helv. Chim. Acta*, **11**, 496 (1928); (b) Ruzicka, Stoll, and Schinz, *Helv. Chim. Acta*, **11**, 670 (1928).

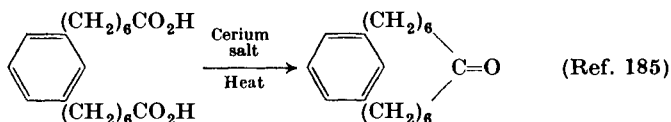
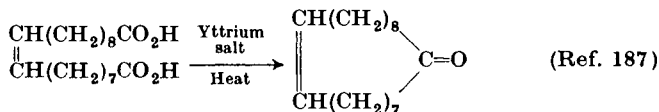
¹⁸⁵ Ruzicka, Buijs, and Stoll, *Helv. Chim. Acta*, **15**, 1220 (1932).

¹⁸⁶ Ruzicka, Brugger, Pfeiffer, Schinz, and Stoll, *Helv. Chim. Acta*, **9**, 499 (1926).

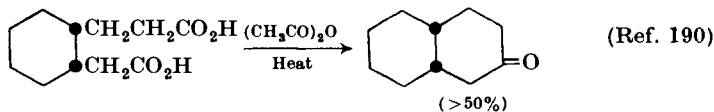
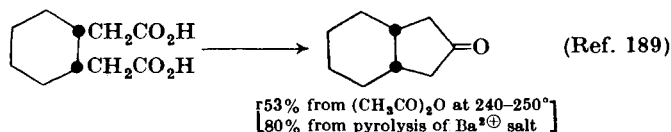
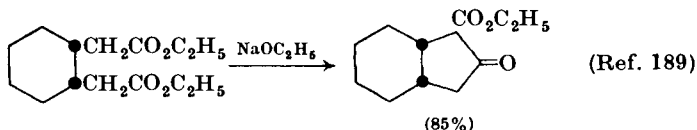
¹⁸⁷ Ruzicka, Stoll, Scherrer, Schinz, and Seidel, *Helv. Chim. Acta*, **15**, 1459 (1932).

¹⁸⁸ Ruzicka, *Ber.*, **50**, 1362 (1917).

the large number of impurities, the method was an important one for many years because it was the only available route to large-ring ketones and the hydrocarbons derived from them. Two examples of the method are shown in the accompanying equations.



Heating an acid with acetic anhydride or pyrolyzing the barium salt is sometimes a useful alternative, as the examples show.



Pyrolysis of a lead salt has been used in the cyclization of a steroid D ring.¹⁹¹ Pyrolysis of adipic acid in the presence of potassium fluoride produces cyclopentanone in yields that vary with the ratio of acid to salt.¹⁹² The reported cyclization of 2,2,5,5-tetramethyladipic acid to 2,2,5,5-tetramethylcyclopentanone under these conditions¹⁹² has been shown to be incorrect. The product is 3,6,6-trimethylcyclohexen-2-one.^{192a}

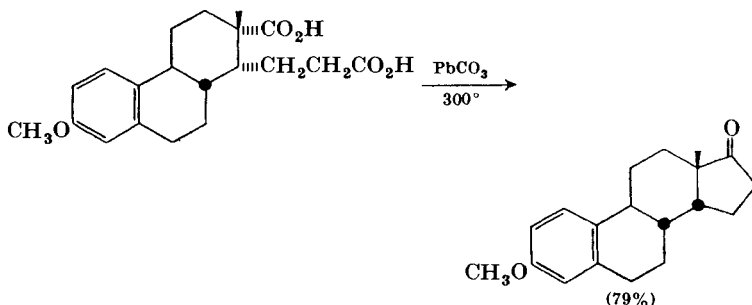
¹⁸⁹ Hückel and Friedrich, *Ann.*, **451**, 132 (1927).

¹⁹⁰ Hückel, *Ann.*, **441**, 14 (1925).

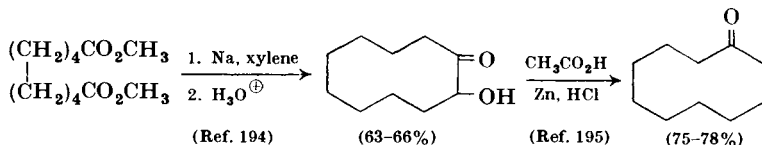
¹⁹¹ Johnson, Christiansen, and Ireland, *J. Am. Chem. Soc.*, **79**, 1995 (1957).

¹⁹² Rand, Wagner, Warner, and Kovac, *J. Org. Chem.*, **27**, 1034 (1962).

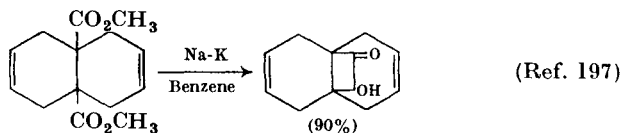
^{192a} Eberson, *Tetrahedron Letters*, **1966**, 223.



The acyloin condensation of dicarboxylic esters is the most useful method for the synthesis of medium- and large-ring ketones. Whereas the Dieckmann and Thorpe-Ziegler condensations are virtually ineffective for rings in the C_9 - C_{12} range, the acyloin condensation followed by a reduction step produces ketones in yields starting at 27% for cyclononane and rapidly improving with increasing ring size.¹⁹³ (See Table I, p. 36.) The initial cyclization usually proceeds in high yield, but reduction of the hydroxy ketone to the ketone is sometimes difficult.



Although only one example of the formation of a four-membered ring in the acyloin condensation has been reported,¹⁹⁶ it is likely that a 1:1 sodium-potassium alloy in refluxing benzene may prove to be a satisfactory combination for general use in the synthesis of small-ring acyloins.¹⁹⁷



The acyloin condensation has been reviewed in *Chemical Reviews*¹⁹⁸ and in *Organic Reactions*.¹⁹⁹

In 1947 and 1948 Blomquist published the details of a method for the synthesis of large-ring ketones from the dichlorides of α,ω -dicarboxylic

¹⁹³ Leonard and Owens, *J. Am. Chem. Soc.*, **80**, 6039 (1958).

¹⁹⁴ Allinger, *Org. Syntheses*, Coll. Vol. **4**, 840 (1963).

¹⁹⁵ Cope, Barthel, and Smith, *Org. Syntheses*, Coll. Vol. **4**, 218 (1963).

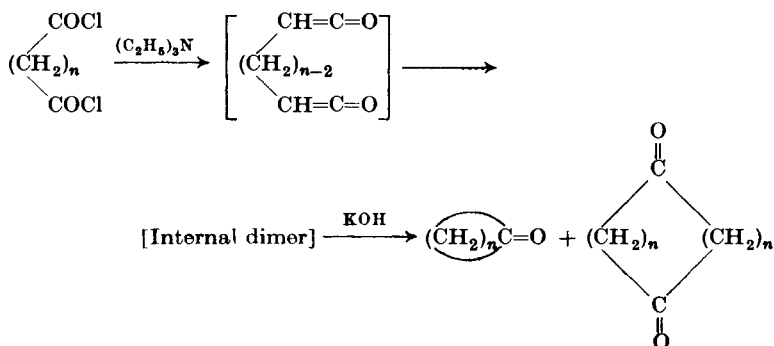
¹⁹⁶ Cope and Herrick, *J. Am. Chem. Soc.*, **72**, 983 (1950).

¹⁹⁷ J. J. Bloomfield and J. R. S. Ireland, Unpublished work.

¹⁹⁸ Finley, *Chem. Rev.*, **64**, 573 (1964).

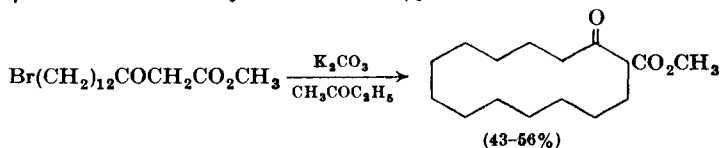
¹⁹⁹ McElvain, *Org. Reactions*, **4**, 256 (1948).

acids *via* diketenes.²⁰⁰⁻²⁰² The reaction has the disadvantage that it is reversible at the ketene dimer stage which leads to polymers, must be run in small batches under high-dilution conditions, and produces fair amounts of dimeric diketenes. Civetone and *dl*-muscone were synthesized in 33% and 22% yields, respectively.²⁰²



Ring enlargement of ketones by reaction with diazomethane may be useful in some cases. Cyclobutanone can be prepared in yields as high as 75% from diazomethane and ketene.²⁰³⁻²⁰⁵ The reaction has been reviewed.²⁰⁶

Another reaction with considerable potential, but seldom used, was discovered by Hunsdiecker. Cyclization, under high-dilution conditions, of ω -bromo- β -ketonic esters with potassium carbonate produces C_{14} - C_{17} cyclic- β -ketonic esters in yields of 40-75%.^{207,208}



House and Babad have reported a new method for preparing C_5 - C_7 cyclic ketones that could have general applicability if it were used under high-dilution conditions.²⁰⁹ Treatment of an ω -iodo ester with triphenylphosphine, followed by reaction with base and hydrolysis of the resulting

²⁰⁰ Blomquist and Spencer, *J. Am. Chem. Soc.*, **69**, 472 (1947).

²⁰¹ Blomquist and Spencer, *J. Am. Chem. Soc.*, **70**, 30 (1948).

²⁰² Blomquist, Holley, and Spencer, *J. Am. Chem. Soc.*, **70**, 34 (1948).

²⁰³ Lipp, Buchkremer, and Seeles, *Ann.*, **499**, 1 (1932).

²⁰⁴ Lipp and Köster, *Ber.*, **64**, 2823 (1931).

²⁰⁵ Kaarsemaker and Coops, *Rec. Trav. Chim.*, **70**, 1033 (1951).

²⁰⁶ Gutsche, *Org. Reactions*, **8**, 377 (1954).

²⁰⁷ Hunsdiecker, *Ber.*, **75**, 1190 (1942).

²⁰⁸ Hunsdiecker, *Ber.*, **75**, 1197 (1942).

²⁰⁹ House and Babad, *J. Org. Chem.*, **28**, 90 (1962).

ylid produces the ketone in 76%, 75%, and 42% yields for C_5 , C_6 , and C_7 ketones, respectively. This reaction, like the preceding one, suffers from the general unavailability of the starting materials and from the excessive amount of time (4 days) required to complete the sequence.

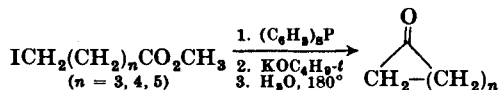


Table I provides a comparison of the most efficient methods for preparing cyclic ketones with the yields obtained by the Dieckmann and Thorpe-Ziegler procedures. The yields reported are for the ketone

TABLE I
COMPARISON OF METHODS FOR PREPARING CYCLIC KETONES²¹⁰ $(\text{CH}_2)_n\text{C}_n\text{O}$

Ring Size $n + 1$	Preferred Method (Yield, %)	Dieckmann (Yield, %)	Thorpe-Ziegler (Yield, %)
4	CH_2N_2 (75) on $\text{CH}_2=\text{C}=\text{O}$	—	—
5	Dieckmann (80)	—	—
6	Dieckmann (60)	—	—
7	Thorpe-Ziegler (70)	(47)	—
8	Thorpe-Ziegler (76)	(15)	—
9	CH_2N_2 on cyclooctanone (61)	(0)	(2.8)
10	Acyloin (50)	(0)	(0.4)
11	Acyloin (53)	(0.5)	(1.4)
12	Acyloin (68)	(0.5)	(8)
13	Acyloin (59)	(24)	(15)
14	Acyloin (75)	(32)	(62)
15	Thorpe-Ziegler (60)	(48)	—

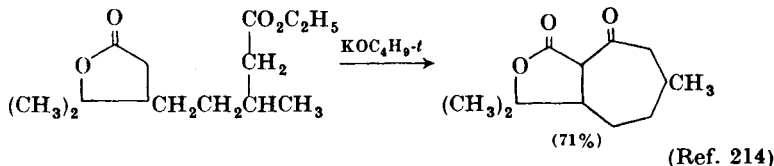
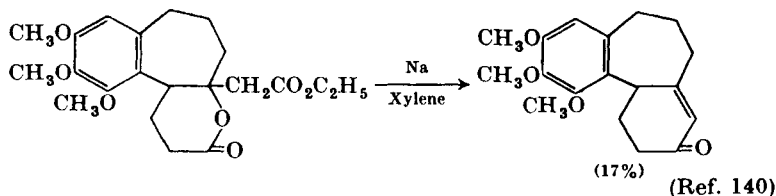
produced after hydrolysis and decarboxylation in the Dieckmann and Thorpe-Ziegler condensations and after reduction of the acyloin condensation product. In this regard it is worth mentioning that a graph of the yield of cyclization product versus ring size that appears in publications by Ziegler^{168, 171} indicates that 5–7 rings are formed in 95–97% yields. The graph is misleading because the yield for some of the other points is based on the amount of cyclic ketone actually obtained. For the first three or four compounds, C_5 – C_8 , the yields are of the enamionitrile. For example, while azelanitrile produces an 89% yield of cyclization product, hydrolysis to the ketone proceeds in only 85% yield (76% overall).

²¹⁰ This table is adapted from one appearing in Ref. 49.

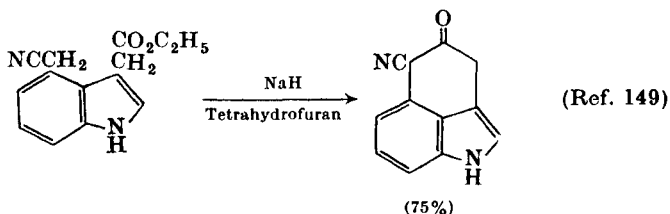
EXPERIMENTAL CONSIDERATIONS

Ethyl esters are used more frequently in the Dieckmann condensation than any others. Increasing the size and complexity of the alkoxy group may lower the yield. With adipic esters the following conversions have been obtained: methyl, 81%; isobutyl, 61%; and benzyl, 57%.²¹¹ Unpublished studies indicate that phenyl esters are generally unreactive.²¹² This observation is in contrast with their behavior in mixed ester-ketone condensations where phenyl esters have been used because of their higher reactivity.²¹³

In a very few instances one of the ester groups is present as a lactone.



One of the ester groups can be replaced with an amide or a nitrile function. Cyclization occurs readily, the ester group providing the carbonyl group of the ketone. When a nitrile group is present, the condensation is part Dieckmann and part Thorpe-Ziegler condensation. Examples of this type of cyclization have been cross-referenced in the tables.

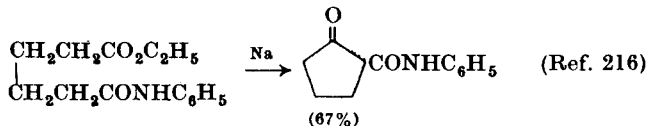
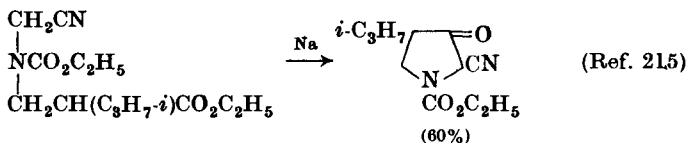


²¹¹ Walther, Treibs, and Michaelis, *Chem. Ber.*, **89**, 60 (1956).

²¹² J. P. Schaefer and M. Moran, Unpublished results.

²¹³ Hauser, Swamer, and Adams, *Org. Reactions*, **8**, 112 (1954).

²¹⁴ Narang and Dutta, *J. Chem. Soc.*, **1964**, 1119.

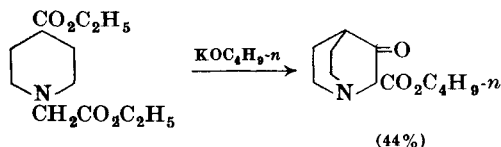


The same solvent and base combinations that are effective in the acetoacetic ester condensation are generally equally effective in the Dieckmann condensation. These and other experimental features which were considered in detail by Hauser and Hudson⁸ need not be repeated.

Sodium hydride is a particularly useful base because (a) it reacts irreversibly with the ester and with the ketonic ester, forming enolates and hydrogen; (b) it has a low molecular weight; and (c) it is easy and relatively safe to handle. The mineral oil in which the sodium hydride is dispersed is readily removed by following one of the procedures described in the next section.

Potassium *t*-butoxide in xylene has found particular utility as a base-solvent combination in reactions leading to large rings.^{49, 51, 58-68} In these reactions the yield is improved not only by using a high-dilution cycle to reduce bimolecular reactions, but also by removing the alcohol formed in the cyclization step by azeotropic distillation with the solvent. Removal of alcohol in this fashion in order to shift the equilibrium in favor of the product should be used in every Dieckmann cyclization, regardless of the base being used.^{129, 131, 133}

A technique which might find special utility in some cases involves the use of potassium hydroxide and *n*-butanol in toluene. The mixture is heated under reflux until no more water separates.²¹⁷ The solution so prepared has been used to cyclize ethyl 4-carbethoxypiperidinoacetate.²¹⁷



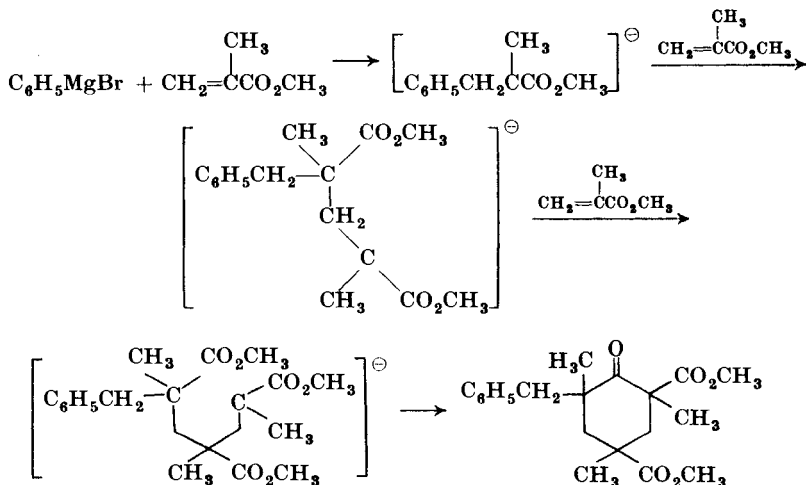
²¹⁵ Miyamoto, Sugawa, Morimoto, Uchibayashi, Sanno, and Tanaka, *Yakugaku Zasshi*, **77**, 571 (1957) [*C.A.*, **51**, 16422i (1957)].

²¹⁶ Johnson, *J. Chem. Soc.*, **1958**, 1624.

²¹⁷ Mikhлина, Rubtsov, and Vorob'eva, *Zh. Obshch. Khim.*, **31**, 3251 (1961); *J. Gen. Chem. USSR (English Transl.)*, **31**, 3033 (1961) [*C.A.*, **57**, 2192e (1962)].

Dimethyl sulfoxide (DMSO) has been suggested as a solvent for Dieckmann^{157, 218} and Thorpe¹⁵⁷ condensations, but it suffers from several disadvantages. The first is that only the equilibrium product mixture can be obtained. Second, unless the reaction mixture is kept cool, the solvent can enter into a variety of side reactions with the ester. Furthermore, when molecules containing isolated double bonds are being cyclized, there is a good possibility that the strongly basic solution will bring about migration of a double bond.²¹⁹ Even cyanide ion may be a strong enough base in DMSO to bring about double-bond migration.²²⁰

The following unusual reaction demonstrates the use of a Grignard reagent as a base in a reaction that, after three Michael-type condensations, leads to a Dieckmann product.²²¹



Many examples of the effect of base, temperature, and solvent on the yield or direction of ring closure have already been described. Because of the importance of these effects several additional examples are presented in this section for emphasis.

In the synthesis of equilenin, the D ring was closed by cyclization of the dicarboxylic ester **72**²²² (p. 40). When sodium was used as the base, the yield was 40–50%, while sodium methoxide produced a yield of 95–98%. The low yield with sodium was traced to caking of the reaction product on the surface of the metal.

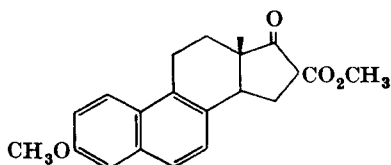
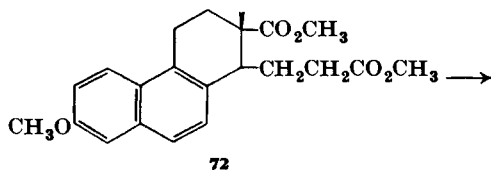
²¹⁸ Gianturco, Friedel, and Giammarino, *Tetrahedron*, **20**, 1763 (1964).

²¹⁹ Schriesheim, Hofmann, and Rowe, *J. Am. Chem. Soc.*, **83**, 3731 (1961).

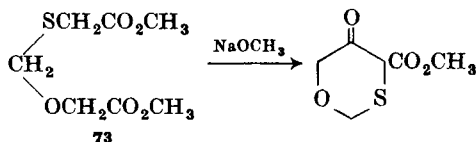
²²⁰ J. J. Bloomfield, Unpublished observations.

²²¹ Owens, Myers, and Zimmerman, *J. Org. Chem.*, **26**, 2388 (1961).

²²² Bachmann, Cole, and Wilds, *J. Am. Chem. Soc.*, **62**, 824 (1940).



The cyclization of the indole derivative shown on p. 37 with tetrahydrofuran as solvent does not occur in diethyl ether.¹⁴⁹ Apparently a higher-boiling solvent is necessary. However, raising the temperature can also lower the yield. In the synthesis of diethyl 2-methyl-3-oxo-1,4-cyclopentanedecarboxylate, described on p. 44, the yield is decreased by as much as 30% if the reaction is conducted in ether at reflux instead of at 0°.²²³ A similar change occurs in the cyclization of 73. At 0° in ether the yield is 43%, while in toluene at 80° the yield is only 22%.²²⁴



EXPERIMENTAL PROCEDURES

All Dieckmann reactions should be carried out under an inert atmosphere; dry, oxygen-free nitrogen is normally used. All the procedures described here are conducted in such an inert atmosphere. The equipment should be dried before assembly. When benzene or an alkylbenzene is used as the solvent, the last traces of water in the equipment and the solvent can be removed by distilling a portion of the solvent before adding any of the reactants. Solvents are best dried by distilling them from calcium hydride, by passing them through a column of molecular sieves, or by a combination of these procedures.

Many reactions, particularly those involving medium- and large-ring syntheses, are best conducted under high-dilution conditions. A creased or Morton flask fitted with a high-speed stirrer, a diluting head, a Hershberg dropping funnel, and a large capacity reflux condenser is used in

²²³ Newman and McPherson, *J. Org. Chem.*, **19**, 1717 (1954).

²²⁴ Brehm and Levenson, *J. Am. Chem. Soc.*, **76**, 5389 (1954).

these reactions. Wiberg has described all the necessary equipment and the experimental procedure.²²⁵ The equipment is available commercially.

For the preparation of metal dispersions a stirrer which operates at speeds up to 20,000 r.p.m. and which provides a particle size of less than 10 μ is available.²²⁶

Sodium hydride is a particularly useful base in Dieckmann and related reactions, but it is available commercially only as a mineral oil dispersion. When high-boiling reaction products are purified only by distillation, any mineral oil originally present will be found as a contaminant in the products. For this reason it is frequently desirable to remove the oil before using the hydride. Because the oil-free hydride is pyrophoric, particularly in moist air, it is necessary to employ an inert atmosphere. The first two procedures for removing oil described below have been found useful in the authors' laboratories.

Oil-Free Sodium Hydride. Method A (*To be used when it is desired to add small amounts of the hydride to a reaction mixture*). The required amount of hydride is quickly transferred to an addition funnel that has a large-bore (3–4 mm.) stopcock and a pressure-equalizing side arm. Dry benzene (or hexane) is added, about 100–150 ml. for each mole of hydride, and the mixture is stirred with a long filter stick made from a coarse 10-mm. sintered disk fused to the end of a piece of 10-mm. glass tubing.²²⁷ The filter stick is passed through a rubber slip joint on an adapter²²⁸ with a side tubulature for a nitrogen inlet. Stirring is accomplished by a combined pumping and side-to-side jiggling motion. After thorough mixing is attained (20–30 seconds) the hydride is allowed to settle and the solvent is removed through the filter stick, by applying aspirator suction, until a fairly dry cake remains. This procedure is repeated at least three more times. The hydride is finally added to the reaction as a slurry in the desired solvent.

Method B. The hydride dispersion is placed in a three-necked flask with a coarse 30-mm. sintered disk built into the bottom and connected to a stopcock.²²⁹ Benzene is added and the mixture is mechanically stirred for about 20 seconds. Then the solvent is removed through the disk by applying gentle aspirator suction. The procedure is repeated at least three more times. The reaction can then be conducted in the flask, or an appropriate solvent can be added and the slurry transferred to another reaction vessel. A 12-mm. U-tube fitted into one of the necks of

²²⁵ Wiberg, *Laboratory Techniques in Organic Chemistry*, McGraw-Hill, New York, 1960, pp. 195, 205, 206, 208, 218.

²²⁶ Lab-Line Stir-O-Vac, Cat. No. 1280, Lab-Line Instruments, Inc. Melrose Park, Ill.

²²⁷ Labglass Incorporated, Vineland, N.J., Catalog LG-61, No. ML 1090.

²²⁸ Labglass, Cat. No. LG 1270.

²²⁹ Labglass, Cat. No. LG 7950.

the flask facilitates transfer of the slurry without exposing it to the air. This procedure is faster than the one described above and is better when large quantities of dispersion are used. Up to 4 moles of sodium hydride have been made oil-free in this way.

Method C. The sodium hydride dispersion is placed in the reaction flask, and then dry benzene or hexane is added. The mixture is swirled, the hydride is allowed to settle, and the solvent is removed by decantation or with the aid of a pipet. This procedure, repeated at least four more times, is faster but is less safe, usually does not completely remove the oil, and allows some of the hydride to be carried out with the washing solvent, so that an excess must be used.

2-Carbethoxycyclopentanone. Several methods, with variations, for the synthesis of this ketonic ester are described in *Organic Syntheses*,²³⁰ this reference should be consulted if the synthesis of any five-membered ring is being attempted, because the methods outlined represent a cross section of workable procedures.

Cycloheptanone.²¹² A 2-l., three-necked, creased flask is fitted for a high-dilution reaction. Toluene (700 ml.) is distilled from calcium hydride directly into the flask, and 12 g. (0.5 mole) of oil-free sodium hydride and 2-3 ml. of absolute *t*-butyl alcohol are added. Heating and stirring are started and, after the toluene begins to boil vigorously, 40.4 g. (0.2 mole) of dimethyl suberate in 750 ml. of dry toluene is added through the Hershberg funnel at a rate of 2-3 drops per minute. Three days are required to complete the addition. The reaction mixture is heated under reflux for 2-3 hours more after the addition is completed.

The solution is cooled and acidified cautiously with acetic acid and water. The toluene layer is separated after washing with water and concentrated to a syrup to which are added 100 ml. of methanol, 50 ml. of water, and 50 ml. of concentrated hydrochloric acid. The solution is heated under reflux for 12 hours, poured onto ice, extracted with diethyl ether, dried, and distilled. Cycloheptanone (12.3-13.0 g.) is obtained as a colorless liquid, b.p. 65-66°/10 mm., in 55-58% yield.

1-Methyl-3-carbethoxy-4-piperidone Hydrochloride.¹³³ In a 500-ml. three-necked flask fitted with a Vigreux column and a mechanical stirrer are placed 250 ml. of dry benzene, 46 g. (0.2 mole) of methyl-*bis*-(β -carbethoxyethyl)amine, and 13.6 g. (0.2 mole) of sodium ethoxide. The reaction mixture is then heated to boiling and the azeotropic mixture of benzene and ethanol distilled until all the ethanol has been removed. Benzene is added, and distillation is repeated until no more ethanol is obtained as evidenced by the refractive index of the distillate (benzene).

²³⁰ Pinkney, *Org. Syntheses*, Coll. Vol. 2, 116 (1943).

The major portion of the benzene is then distilled from the reaction mixture, and 120 ml. of water is added. The aqueous phase is extracted with diethyl ether and acidified to Congo red in the cold with hydrochloric acid, made alkaline with potassium carbonate, and extracted with diethyl ether until a negative ferric chloride test is given by the extract. The extracts are concentrated to about 250 ml., and dry hydrogen chloride is introduced to precipitate the hydrochloride. The yield is 29.2 g. (71%), m.p. 128–129°.

3-Hydroxy-2,5-dicarbomethoxythiophene.⁸⁰ In a 500-ml. three-necked flask equipped with a stirrer, condenser, and dropping funnel is placed 5.4 g. (0.1 mole) of sodium methoxide in 50 ml. of dry benzene. A solution of 10.6 g. (0.1 mole) of methyl thioglycolate in 150 ml. of dry benzene is added under an atmosphere of nitrogen and is followed by dropwise addition of 14.2 g. (0.1 mole) of dimethyl acetylenedicarboxylate in 150 ml. of dry benzene. After the reaction mixture has been heated under reflux for 3 hours, water is added and the benzene extracted with cold water. The aqueous layer is cautiously acidified, and 20.5 g. of crude product (94%) is obtained as a crystalline mass. Recrystallization from aqueous methanol gives the product melting at 111°.

2,5-Dimethyl-5-carbomethoxycyclopentanone¹²⁹ (Cyclization, Alkylation, Rearrangement, and Alkylation). A 5-l. three-necked flask fitted with an efficient Hershberg stirrer, a Vigreux column carrying a partial take-off head for distillation, and a dropping funnel is charged with 2 l. of dry xylene and 24.0 g. (1.0 mole) of oil-free sodium hydride. Dimethyl adipate, 174 g. (1.0 mole), is added, and the mixture is stirred and slowly distilled for 3–4 hours until the boiling point reaches 120° and a gas chromatogram of an acidified aliquot shows less than 1% of residual starting material.

The mixture is cooled to room temperature, 213 g. (1.5 moles) of methyl iodide is slowly added, and stirring is continued for 6 hours. Another 71.0 g. (0.5 mole) of methyl iodide is added, and stirring is continued for an additional 10 hours. The mixture is then slowly distilled until the boiling point reaches 120°. The gas chromatogram shows only one product, with retention time identical with that of authentic 2-methyl-2-carbomethoxycyclopentanone. The mixture is cooled to room temperature, and a slurry of 1.0 mole of freshly prepared methanol-free sodium methoxide (prepared from 23 g. of sodium) in 500 ml. of xylene is added. The mixture is heated at reflux for 9 hours and then slowly distilled for 2–5 hours until the boiling point reaches 120–126° and the gas chromatogram shows the presence of only one product; the retention time is identical with that of authentic 5-methyl-2-carbomethoxycyclopentanone.

The mixture is again cooled to room temperature, and 284 g. (2.0 moles)

of methyl iodide is added slowly. After the mixture has been stirred for an additional 12 hours, it is poured onto 1 kg. of ice and 300 ml. of 6*N* hydrochloric acid with vigorous stirring. The layers are separated, the aqueous layer is extracted twice with 50:50 diethyl ether-benzene, and the combined organic layers are washed with saturated aqueous sodium bisulfite and then dried with sodium sulfate. Distillation affords 129–132 g. (76–78%) of the dimethyl ketonic ester, b.p. 108–114°/23–25 mm. The gas chromatogram of this product shows two major components in nearly equal proportions, neither of which corresponds in retention time to any other intermediate in the sequence, and 3–5% of dimethyl α,α' -dimethyladipate. Redistillation affords material of analytical purity (two isomers): b.p. 110–111°/25 mm.

Diethyl 2-Methyl-3-oxo-1,4-cyclopentanedicarboxylate.²²³ In a 5-l. three-necked flask fitted with a stirrer, a Hershberg addition funnel, and a thermometer are placed 97.2 g. (4 moles + 1.2% excess) of oil-free sodium hydride, 2.4 l. of dry diethyl ether, and 5 ml. of absolute ethanol. The contents of the flask are maintained at 0° while 1153 g. (4 moles) of triethyl 4-methyl-1,3,4-pentanetricarboxylate is added over 20 hours with continuous stirring. (When the ether is allowed to boil, the yield is 20–30% less.) The reaction mixture is worked up by adding 1 l. of 6*N* hydrochloric acid and separating the ether layer, which is then washed with 200 ml. of 10% aqueous sodium carbonate. Removal of the ether followed by vacuum distillation gives 892 g. (92%) of product, b.p. 153–156°/6–7 mm.

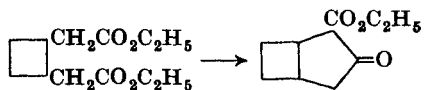
***cis*-Bicyclo[5.2.0]nonan-4-one**⁴⁷ (**High-Dilution Ziegler Condensation Using Lithium *N*-Methyl Anilide**). To a stirred, refluxing mixture of 2.5 l. of dry diethyl ether and 3.5 g. (0.5 g. atom) of lithium contained in a 5-l. flask fitted with a high-dilution apparatus is added 39 g. (0.25 mole) of bromobenzene over 2.5 hours. Then 34 g. (0.32 mole) of *N*-methylaniline is added over 20 minutes, followed by 8.1 g. (0.05 mole) of *cis*-1,2-*bis*-(β -cyanoethyl)cyclobutane in 1 l. of dry diethyl ether added over 48 hours. The reaction mixture is cooled to room temperature and decomposed by the addition of 150 ml. of 3.3*N* hydrochloric acid. After stirring at room temperature for 30 minutes, the organic layer is removed and the aqueous layer is extracted with diethyl ether. The combined ether extracts are evaporated, and the residue is heated under reflux with 200 ml. of 33% sulfuric acid for 3 hours. The ketone is obtained by slow steam distillation (24 hours), ether extraction of the distillate, drying over anhydrous magnesium sulfate, filtration, evaporation of the ether, and distillation, 5.0 g. (72%), b.p. 100–104°/30–40 mm., n_D^{25} 1.4876.

2-Cyano-5-phenylcyclooct-1-enylamine¹⁶¹ (**High-Dilution Ziegler Condensation Employing Sodium *N*-Methyl Anilide**). Sodium

methyl anilide is prepared by heating under reflux for 4 hours with vigorous stirring a mixture of 40.4 g. of naphthalene, 12 g. of sodium wire, 70 g. of methylaniline, and 800 ml. of anhydrous diethyl ether contained in a 3-l. three-necked flask fitted for a high-dilution reaction. Then 11.8 g. of 5-phenylazelanitrile in 250 ml. of anhydrous diethyl ether is added over 8 hours. The reaction mixture is heated under reflux for 1 hour, cooled, and cautiously treated with 750 ml. of water with stirring and cooling. The ethereal layer is separated, and the aqueous layer is extracted with 250 ml. of diethyl ether. The ether is evaporated, and the residue is steam-distilled to remove naphthalene, dihydronaphthalene, and methylaniline. The material remaining after the steam distillation is extracted with diethyl ether, and the ethereal solution is dried over anhydrous magnesium sulfate and then concentrated. The remaining oil is dissolved in dry diethyl ether and ethanol and, upon cooling at -80° , the crystalline enamine is deposited. Successive concentrations and coolings of the mother liquor produce a total of 6.4 g. (54%), m.p. $87.4-96.6^{\circ}$. Recrystallization from absolute ethanol gives the pure compound, m.p. $96.8-98.0^{\circ}$.

TABULAR SURVEY*

An attempt has been made to include in the tables all the Dieckmann and Thorpe-Ziegler condensations reported through June 1964; there are some references through March 1965. The reactions are listed in each table according to the size of the ring formed in the condensation. Thus the cyclization



would be listed under condensations leading to the formation of a five-membered ring. This arrangement has been selected as the most helpful in finding whether a particular product has been prepared by a Dieckmann condensation. When rings of different sizes are prepared in the same condensation, the reaction is listed under each ring size and cross-referenced.

Within each group of reactions in which the ring formed is of the same size, the entries are arranged according to the numbers of C, H, and O atoms in the starting *acid*. The esters are listed by the number of carbon atoms in the acid, the methyl ester being followed by the ethyl ester,

* We are indebted to our graduate students, too many to mention individually, who helped us check the tables for accuracy.

propyl ester, and so on. Consequently, ethyl cyclopentanone-2-carboxylate precedes the benzyl ester. Each product actually isolated, whether it is the ketonic ester, the alkylated ketonic ester, or the ketones derived from either of these, is listed after the acyclic ester from which it is derived. This system avoids multiple entries for the same starting ester but means that, in looking for a given *product*, all possible precursors must be considered. In reactions for which more than one reference is cited, the experimental data are taken from the first reference and the remaining references are arranged in numerical order.

TABLE I
COMPARISON OF METHODS FOR PREPARING CYCLIC KETONES²¹⁰ $(\text{CH}_2)_n\text{C}_n\text{O}$

Ring Size $n + 1$	Preferred Method (Yield, %)	Dieckmann (Yield, %)	Thorpe-Ziegler (Yield, %)
4	CH_2N_2 (75) on $\text{CH}_2=\text{C}=\text{O}$	—	—
5	Dieckmann (80)		—
6	Dieckmann (60)		—
7	Thorpe-Ziegler (70)	(47)	
8	Thorpe-Ziegler (76)	(15)	
9	CH_2N_2 on cyclooctanone (61)	(0)	(2.8)
10	Acyloin (50)	(0)	(0.4)
11	Acyloin (53)	(0.5)	(1.4)
12	Acyloin (68)	(0.5)	(8)
13	Acyloin (59)	(24)	(15)
14	Acyloin (75)	(32)	(62)
15	Thorpe-Ziegler (60)	(48)	

TABLE II
CONDENSATIONS LEADING TO CARBOCYCLIC PRODUCTS

A. Condensations Leading to Four-Membered Rings				
Starting Ester	Product(s)	Base	Yield (%)	Refs.
$C(CH_3)_2CO_2C_2H_5$ $CH(CO_2C_2H_5)CH_2CO_2C_2H_5$	$(CH_3)_2C=O$ $C_2H_5O_2C$	Na	(0)	441
$C(C_2H_5)_2CH_2CO_2CH_3$ $CH_2CO_2CH_3$	$(C_2H_5)_2C=O$ CO_2CH_3	NaOCH ₃	(Low)	240
 $CH(CO_2C_2H_5)CH_2CO_2C_2H_5$		Na	(0)	441
 $CH_2CO_2C_2H_5$		K	(1)	314
 $CH(CO_2C_2H_5)CH_2CO_2C_2H_5$		Na	(1)	441

Note: References 231 to 583 are on pp. 197-203.

^a This product was isolated after hydrolysis and decarboxylation.

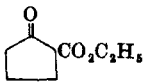
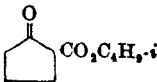
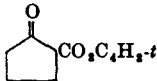
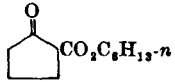
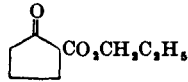
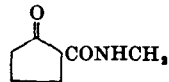
^b The carbon-hydrogen analysis was poor.

TABLE II—Continued
CONDENSATIONS LEADING TO CARBOCYCLIC PRODUCTS

A. Condensations Leading to Four-Membered Rings—Continued				
Starting Ester	Product(s)	Base	Yield (%)	Refs.
CH_3 $CH(CO_2C_2H_5)CH_2CO_2C_2H_5$	CH_3	Na	(1)	441
 $CH_2CO_2C_2H_5$ $CH_2CO_2C_2H_5$ CH_3	A B C	Na:K	(A, 5.6) (B, 24) (C, 26)	34

B. Condensations Leading to Five-Membered Rings

C_3H_{10} $CH_2CH_2CO_2CH_3$ $CH_2CH_2CO_2CH_3$		Na NaNH ₂	(74-81) (—)	211 420
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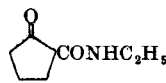
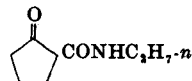
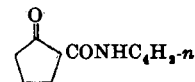
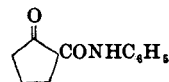
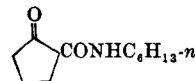
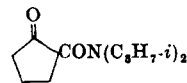
$\begin{array}{c} \text{CH}_2\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5 \\ \\ \text{CH}_2\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5 \end{array}$		Na (60-90) Mg(OC ₂ H ₅) ₂ (—) NaOC ₂ H ₅ (70) NaH (65-75) NaNH ₂ (60)	232, 1, 16, 40, 130, 132, 230, 263, 360, 455, 456 352 365, 14 157 263, 357, 417
$\begin{array}{c} \text{CH}_2\text{CH}_2\text{CO}_2\text{C}_4\text{H}_9-i \\ \\ \text{CH}_2\text{CH}_2\text{CO}_2\text{C}_4\text{H}_9-i \end{array}$		Na (75)	211
$\begin{array}{c} \text{CH}_2\text{CH}_2\text{CO}_2\text{C}_4\text{H}_9-t \\ \\ \text{CH}_2\text{CH}_2\text{CO}_2\text{C}_4\text{H}_9-t \end{array}$		NaNH ₂ (80)	475
$\begin{array}{c} \text{CH}_2\text{CH}_2\text{CO}_2\text{C}_6\text{H}_{13}-n \\ \\ \text{CH}_2\text{CH}_2\text{CO}_2\text{C}_6\text{H}_{13}-n \end{array}$		Na (61)	211
$\begin{array}{c} \text{CH}_2\text{CH}_2\text{CO}_2\text{CH}_2\text{C}_6\text{H}_5 \\ \\ \text{CH}_2\text{CH}_2\text{CO}_2\text{CH}_2\text{C}_6\text{H}_5 \end{array}$		Na (57)	211
$\begin{array}{c} \text{CH}_2\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5 \\ \\ \text{CH}_2\text{CH}_2\text{CONHCH}_3 \end{array}$		Na (10)	216

Note: References 231 to 583 are on pp. 197-203.

^b The carbon-hydrogen analysis was poor.

TABLE II—Continued
CONDENSATIONS LEADING TO CARBOCYCLIC PRODUCTS

B. Condensations Leading to Five-Membered Rings—Continued

Starting Ester	Product(s)	Base	Yield (%)	Refs.
C ₈ H ₁₆ (contd.)				
$\begin{array}{c} \text{CH}_2\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5 \\ \\ \text{CH}_2\text{CH}_2\text{CONHC}_2\text{H}_5 \end{array}$		Na	(38)	216
$\begin{array}{c} \text{CH}_2\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5 \\ \\ \text{CH}_2\text{CH}_2\text{CONHC}_6\text{H}_{13}-n \end{array}$		Na	(47)	216
$\begin{array}{c} \text{CH}_2\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5 \\ \\ \text{CH}_2\text{CH}_2\text{CONHC}_4\text{H}_9-n \end{array}$		Na	(65)	216
$\begin{array}{c} \text{CH}_2\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5 \\ \\ \text{CH}_2\text{CH}_2\text{CONHC}_6\text{H}_5 \end{array}$		Na	(67)	216
$\begin{array}{c} \text{CH}_2\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5 \\ \\ \text{CH}_2\text{CH}_2\text{CONHC}_6\text{H}_{13}-n \end{array}$		Na	(62)	216
$\begin{array}{c} \text{CH}_2\text{CH}_2\text{CO}_2\text{CH}_3 \\ \\ \text{CH}_2\text{CH}_2\text{CON}(\text{C}_2\text{H}_5-i)_2 \end{array}$		NaOCH ₃	(41)	211

$C_7H_{10}-C_7H_{12}$			$NaOC_2H_5$ in C_2H_5OH (66)	131
			$NaOC_2H_5$ in $C_6H_5CH_3$ (85) ^c	131
			Na (79)	500
$CH_2CO_2C_2H_5$ $CHCO_2C_2H_5$ $CH_2CH_2CO_2C_2H_5$	A		Na (A + B, 45-84)	103, 104, 105, ^d 106
	B		(A, 66) (B, 12)	107
$CH_2CH(CH_3)CO_2C_2H_5$ $CH_2CH_2CO_2C_2H_5$			Na (70-80)	263, 15, 245, 360, 364
			$NaOC_2H_5$ (65)	131, 14
			$NaNH_2$ (—)	358, 420
$CH(CH_3)CH_2CO_2C_2H_5$ $CH_2CH_2CO_2C_2H_5$	A	and some B, see p. 52	Na (60-80)	17, 97-99
			$NaNH_2$ (71-74)	100

Note: References 231 to 583 are on pp. 197-203.

^c Alcohol was removed by azeotropic distillation with the solvent.

^d The reaction was solvent-temperature dependent. The following ratios of A:B were obtained: in ether, 2.6:1; in benzene, 3.4:1; in xylene, 4.5:1.

TABLE II—Continued
CONDENSATIONS LEADING TO CARBOCYCLIC PRODUCTS

B. Condensations Leading to Five-Membered Rings—Continued

Starting Ester	Product(s)	Base	Yield (%)	Refs.
$C_7H_{10}-C_7H_{12}$ (contd.)				
	B	$NaOC_2H_5$	(—)	101, 14, 96 ^a
C_8H_{10}				
		KOC_2H_5	(—)	384
		$NaOC_2H_5$ in C_2H_5OH	(75) ^f	121, 120, 418
		$NaOC_2H_5$ in C_6H_6	(Low) ^f	121
$CH_2CH(CO_2C_2H_5)_2$ $CH_2CH(CO_2C_2H_5)_2$	A	$NaOC_2H_5$	(A, 31-63) (B, 15)	23, 25, 27, 30 23
	B	Na	(A, 69)	26

$\text{CH}_3\text{CH}(\text{CO}_2\text{C}_2\text{H}_5)_2$ $\text{CH}(\text{CO}_2\text{C}_2\text{H}_5)\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5$		NaOC_2H_5	(66)	493
$\text{CH}_3\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5$ $\text{C}(\text{CO}_2\text{C}_2\text{H}_5)_2$ $\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5$	A	Na	(A + B, 70-83)	105-107
	B	NaOC_2H_5	(A + B, 33)	106
C_2H_5 		NaOC_2H_5	(87)*	131
		Na	(—)	312
$\text{CH}(\text{CO}_2\text{CH}_3)\text{CH}_2\text{CO}_2\text{CH}_3$ $\text{CH}_3\text{CH}_2\text{CH}_2\text{CO}_2\text{CH}_3$		NaOCH_3 Na	(ⁱ) (^b)	110 110

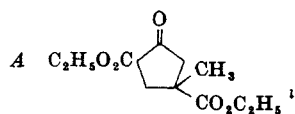
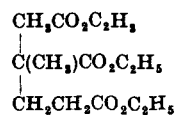
Note: References 231 to 583 are on pp. 197-203.

- * Alcohol was removed by azeotropic distillation with the solvent.
- * The ratio of A to B was found to be at least 4:1.
- * This product is accompanied by isomeric cyclohexanone; see Table II-C.
- * Compound A was also prepared in 23% yield from diethyl malonate and 1,1-dicarbethoxycyclopropane.
- * Diethyl carbonate was also formed.
- * Cyclohexanone isomers were also formed; see Table II-C.
- * The cyclopentanone was 85% of the mixture.
- * The cyclopentanone was 19% of a mixture with 2,3-dicarbethoxycyclohexanone; see Table II-C.

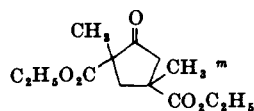
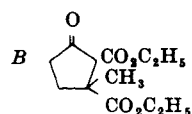
TABLE II—Continued
CONDENSATIONS LEADING TO CARBOCYCLIC PRODUCTS

B. Condensations Leading to Five-Membered Rings—Continued

Starting Ester	Product(s)	Base	Yield (%)	Refs.
C_2H_5 , (contd.)				
$\text{CH}(\text{CO}_2\text{C}_2\text{H}_5)\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5$ $\text{CH}_3\text{CH}_2\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5$		NaOC_2H_5 in $\text{C}_2\text{H}_5\text{OH}$	(Poor) ^c	121, 418
$\text{CH}_3\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5$ $\text{CHCO}_2\text{C}_2\text{H}_5$ $\text{CH}(\text{CH}_3)\text{CO}_2\text{C}_2\text{H}_5$		Na NaOC_2H_5 NaH	(70) (85) (92)	264 107, 476 223
$\text{CH}_3\text{CHCH}_2\text{CO}_2\text{C}_2\text{H}_5$ $\text{CHCO}_2\text{C}_2\text{H}_5$ $\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5$	A	Na	(A or B, 70)	266
	B			
$\text{CH}_3\text{CH}(\text{CH}_3)\text{CO}_2\text{C}_2\text{H}_5$ $\text{CH}(\text{CO}_2\text{C}_2\text{H}_5)\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5$		Na	(Good)	266



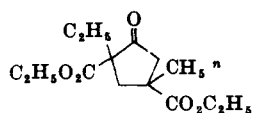
Na

(A, not B,
75-84)112, 113, 124
125

Na

(81)

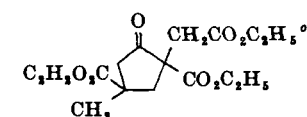
112



Na

(87)

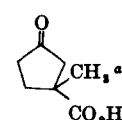
123



Na

(—)

122



Na

(68)

188

Note: References 231 to 583 are on pp. 197-203.

^a This product was isolated after hydrolysis and decarboxylation.

^b Cyclohexanone isomers were also formed; see Table I-C.

^c This is the most probable structure;^{112, 122} see text, pp. 21-22.

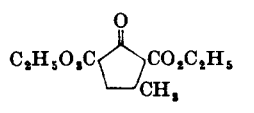
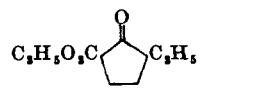
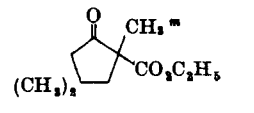
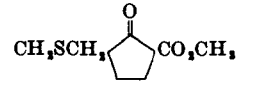
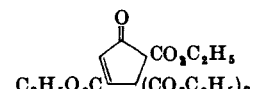
^m The intermediate enolate was alkylated with methyl iodide.

ⁿ The intermediate enolate was alkylated with ethyl iodide.

^o The intermediate enolate was alkylated with ethyl bromoacetate.

TABLE II—Continued
CONDENSATIONS LEADING TO CARBOCYCLIC PRODUCTS

B. Condensations Leading to Five-Membered Rings—Continued

Starting Ester	Product(s)	Base	Yield (%)	Refs.
C_2H_{12} (contd.)				
$\begin{array}{c} \text{CH}_2\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5 \\ \\ \text{CH}_2\text{CHCH}(\text{CO}_2\text{C}_2\text{H}_5)_2 \end{array}$		NaOC_2H_5	(Poor)	97
C_2H_{14}				
$\begin{array}{c} \text{CH}_2\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5 \\ \\ \text{CH}_2\text{CH}(\text{C}_2\text{H}_5)\text{CO}_2\text{C}_2\text{H}_5 \end{array}$		NaOC_2H_5	(—)	14
$\begin{array}{c} \text{CH}_2\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5 \\ \\ \text{C}(\text{CH}_3)_2\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5 \end{array}$		Na	(70)	95
$\begin{array}{c} \text{CO}_2\text{CH}_3 \\ \\ \text{CHCH}_2\text{SCH}_3 \\ \\ (\text{CH}_3)_2\text{CO}_2\text{CH}_3 \end{array}$		Na	(29)	523
$\text{C}_2\text{H}_8-\text{C}_2\text{H}_{10}$				
$\begin{array}{c} \text{CH}_2\text{CO}_2\text{C}_2\text{H}_5 \\ \\ \text{C}(\text{CO}_2\text{C}_2\text{H}_5)_2 \\ \\ \text{C}=\text{CHCO}_2\text{C}_2\text{H}_5 \\ \\ \text{CO}_2\text{C}_2\text{H}_5 \end{array}$		NaOC_2H_5	(—)	299

		Na	(13)	26
		NaOC ₂ H ₅	(78)	130
		NaOC ₂ H ₅	(58)	120
		NaOC ₂ H ₅	(91)	107, 427
		Na	(71)	472
		Na	(—)	423

Note: References 231 to 583 are on pp. 197-203.

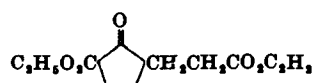
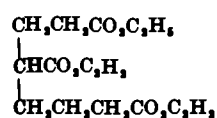
* This product was isolated after hydrolysis and decarboxylation.

** The intermediate enolate was alkylated with methyl iodide.

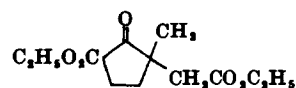
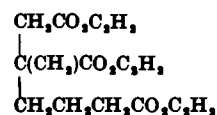
TABLE II—Continued
CONDENSATIONS LEADING TO CARBOCYCLIC PRODUCTS

B. Condensations Leading to Five-Membered Rings—Continued

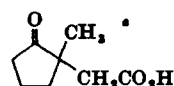
Starting Ester	Product(s)	Base	Yield (%)	Refs.
		NaOC ₂ H ₅	(82)*	131
		Na	(52)	310
		Na	(60)	40
		NaOCH ₃	(A)	231, 362, 424
		Na	(B)	253



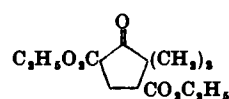
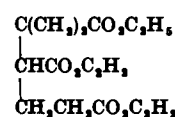
Na (13) 310, 418



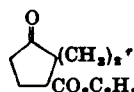
Na (70) 115, 94, 116, 117



Na (50) 118
NaOC₂H₅ (73) 118
NaOCH₃ (30) 118
KOC₂H₅-t (61) 118



Na (70) 261, 392,* 556



Na (76) 525
NaH (76) 375

Note: References 231 to 583 are on pp. 197-203.

- * The product described in this reference was obtained by alkylating the intermediate enolate with ethyl bromoacetate.
- * This product was isolated after hydrolysis and decarboxylation.
- * Alcohol was removed by azeotropic distillation with the solvent.
- * The *trans* isomer did not cyclize.
- * The *trans* isomer gave the same product.
- * This product was isolated after hydrolysis, decarboxylation, and reesterification.

THE DIECKMANN CONDENSATION

59

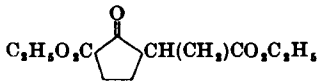
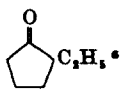
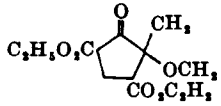
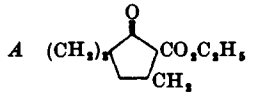
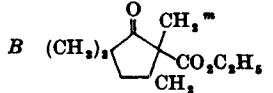
TABLE II—Continued
CONDENSATIONS LEADING TO CARBOCYCLIC PRODUCTS

B. Condensations Leading to Five-Membered Rings—Continued

Starting Ester	Product(s)	Base	Yield (%)	Refs.
C_2H_{14} (contd.)				
$\begin{array}{c} \text{CH}_3\text{CO}_2\text{C}_2\text{H}_5 \\ \\ \text{CHCO}_2\text{C}_2\text{H}_5 \\ \\ \text{C}(\text{CH}_3)_2\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5 \end{array}$	$\begin{array}{c} \text{O} \\ \parallel \\ \text{C} \end{array} \text{C}_2\text{H}_4\text{C}(\text{CH}_3)_2\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5$	Na	(Good)	109
$\begin{array}{c} \text{CH}(\text{CH}_3)\text{CO}_2\text{C}_2\text{H}_5 \\ \\ \text{C}(\text{CH}_3)\text{CO}_2\text{C}_2\text{H}_5 \\ \\ \text{CH}_2\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5 \end{array}$	$\text{C}_2\text{H}_5\text{O}_2\text{C} \begin{array}{c} \text{O} \\ \parallel \\ \text{C} \end{array} \text{C}_2\text{H}_4\text{C}(\text{CH}_3)\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5$	Na	(76)	446
	$\begin{array}{c} \text{O} \\ \parallel \\ \text{C} \end{array} \text{C}_2\text{H}_4\text{C}(\text{CH}_3)_2\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5$	Na	(80)	241, 526
$\begin{array}{c} \text{CH}_3\text{CO}_2\text{C}_2\text{H}_5 \\ \\ \text{C}(\text{CH}_3)\text{CO}_2\text{C}_2\text{H}_5 \\ \\ \text{CH}_2\text{CH}(\text{CH}_3)\text{CO}_2\text{C}_2\text{H}_5 \end{array}$	$\begin{array}{c} \text{O} \\ \parallel \\ \text{C} \end{array} \text{C}_2\text{H}_4\text{C}(\text{CH}_3)\text{CH}(\text{CH}_3)\text{CO}_2\text{C}_2\text{H}_5$	Na	(77)	112
$\begin{array}{c} \text{CH}_3\text{CO}_2\text{C}_2\text{H}_5 \\ \\ \text{C}(\text{CH}_3)\text{CO}_2\text{C}_2\text{H}_5 \\ \\ \text{CH}(\text{CH}_3)\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5 \end{array}$	$\begin{array}{c} \text{O} \\ \parallel \\ \text{C} \end{array} \text{C}_2\text{H}_4\text{C}(\text{CH}_3)\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5$	Na	(—)	391

60

ORGANIC REACTIONS

$\begin{array}{c} \text{CH}(\text{CH}_3)\text{CO}_2\text{C}_2\text{H}_5 \\ \\ \text{CHCO}_2\text{C}_2\text{H}_5 \\ \\ \text{CH}_2\text{CH}_2\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5 \end{array}$		(—)	(—)	406
$\begin{array}{c} \text{CH}_2\text{CH}_2\text{CH}(\text{CO}_2\text{C}_2\text{H}_5)_2 \\ \\ \text{CH}(\text{C}_2\text{H}_5)\text{CO}_2\text{C}_2\text{H}_5 \end{array}$		NaOC_2H_5	(22)	490
$\begin{array}{c} \text{CH}_2\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5 \\ \\ \text{CHCO}_2\text{C}_2\text{H}_5 \\ \\ \text{CH}_2\text{C}(\text{OCH}_2)\text{CO}_2\text{C}_2\text{H}_5 \end{array}$		Na	(—)	529
$\begin{array}{c} \text{C}_2\text{H}_5 \\ \\ \text{CH}(\text{CH}_3)\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5 \\ \\ \text{CH}_2\text{C}(\text{CH}_3)_2\text{CO}_2\text{C}_2\text{H}_5 \end{array}$	<p>A </p> <p>B </p>	NaOC_2H_5	(A, 75)	385
		Na	(B, 89)	127

Note: References 231 to 583 are on pp. 197–203.

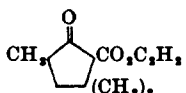
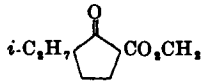
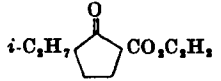
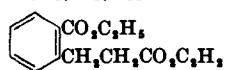
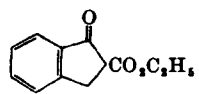
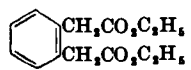
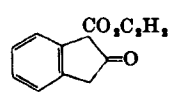
* This product was isolated after hydrolysis and decarboxylation.

^m The intermediate enolate was alkylated with methyl iodide.

^r This product was isolated after hydrolysis, decarboxylation, and reesterification.

TABLE II—Continued
CONDENSATIONS LEADING TO CARBOCYCLIC PRODUCTS

B. Condensations Leading to Five-Membered Rings—Continued

Starting Ester	Product(s)	Base	Yield (%)	Refs.
C_2H_5 (contd.)				
$\begin{array}{c} \text{C}(\text{CH}_3)_2\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5 \\ \\ \text{CH}_2\text{CH}(\text{CH}_3)\text{CO}_2\text{C}_2\text{H}_5 \end{array}$		NaOC_2H_5	(75)	385
		Na	(—)	385
$\begin{array}{c} \text{CH}_2\text{CH}_2\text{CO}_2\text{CH}_3 \\ \\ \text{CH}_2\text{CH}(\text{C}_2\text{H}_5-i)\text{CO}_2\text{CH}_3 \end{array}$		Na	(—)	19
$\begin{array}{c} \text{CH}_2\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5 \\ \\ \text{CH}_2\text{CH}(\text{C}_2\text{H}_5-i)\text{CO}_2\text{C}_2\text{H}_5 \end{array}$		Na	(55)	19
		NaOC_2H_5	(—)	14
		NaNH_2	(66)	359, 420
$\text{C}_{10}\text{H}_{10}-\text{C}_{10}\text{H}_{11}$ 		Na	(Good)	235, 254
		Na	(70–90)	343, 235, 13

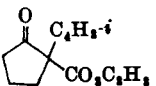
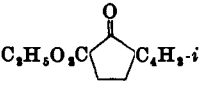
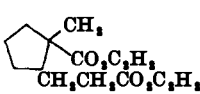
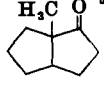
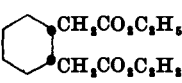
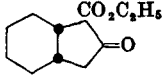
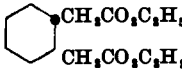
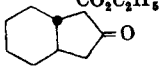
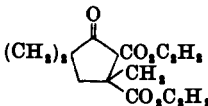
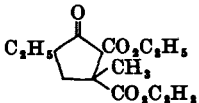
		(0)	146
$\text{CH}_3\text{CH}(\text{CO}_2\text{C}_2\text{H}_5)_2$ $\text{CH}(\text{CH}=\text{CH}_2)\text{CH}(\text{CO}_2\text{C}_2\text{H}_5)_2$		NaOC_2H_5 (50-60)	24, 25
$\text{C}_{10}\text{H}_{14}$ 		NaH in $(\text{CH}_3)_2\text{SO}$ (75)	157
		NaH in $(\text{CH}_3)_2\text{SO}$ (83)	157
$\text{CH}_3\text{CH}_2\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5$ $\text{C}(\text{COCH}_3)\text{CO}_2\text{C}_2\text{H}_5$ $\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5$		NaOC_2H_5 (—)	21

Note: References 231 to 583 are on pp. 197-203.

- * This product was isolated after hydrolysis and decarboxylation.
- * Diethyl carbonate was also formed.
- * Various Dieckmann conditions were tried without success.
- * The starting ester was formed *in situ* from diethyl malonate and diethyl 2-vinylcyclopropane-1,1-dicarboxylate.
- * Ethyl acetate was formed during the reaction.

TABLE II—Continued
CONDENSATIONS LEADING TO CARBOCYCLIC PRODUCTS

B. Condensations Leading to Five-Membered Rings—Continued				
Starting Ester	Product(s)	Base	Yield (%)	Refs.
$\text{C}_{10}\text{H}_{14}$ (contd.) $\text{CH}_3\text{CH}_2\text{CH}(\text{CO}_2\text{C}_2\text{H}_5)_2$ $\text{C}_2\text{H}_5\text{C}(\text{CO}_2\text{C}_2\text{H}_5)_2$		NaOC_2H_5	(74)	23
$\text{CH}_3\text{CO}_2\text{CH}_2$ $\text{C}(\text{CH}_3)\text{CO}_2\text{CH}_2$ $\text{CH}(\text{CO}_2\text{CH}_2)\text{CH}_2\text{CH}_2\text{CO}_2\text{CH}_2$		Na	(Good)	488
$\text{CH}(\text{CO}_2\text{CH}_2)\text{CH}_2\text{CH}_2\text{CO}_2\text{CH}_2$ $\text{CH}(\text{CO}_2\text{CH}_2)\text{CH}_2\text{CH}_2\text{CO}_2\text{CH}_2$		Na	(60)	44, 43
$\text{CH}(\text{CO}_2\text{C}_2\text{H}_5)\text{CH}_2\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5$ $\text{CH}(\text{CO}_2\text{C}_2\text{H}_5)\text{CH}_2\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5$		KOC_4H_9 -t Na	(A, 23-45) (A, 33) (B, 11)	43 105 105

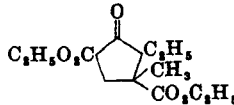
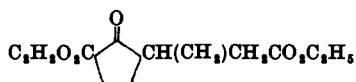
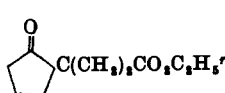
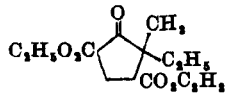
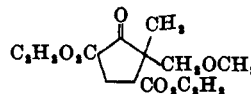
$C_{10}H_{16}$ 		$NaOC_2H_5$	(85) ^a	131
		Na	(51)	126
		$NaOC_2H_5$	(Quant.)	189
		$NaOC_2H_5$	(—)	189
$CH_3C(CH_3)_2CO_2C_2H_5$ $C(CH_3)_2CO_2C_2H_5$ $CH_2CO_2C_2H_5$ $CH_2CO_2C_2H_5$ $C(CH_3)_2CO_2C_2H_5$ $CH_2CH(C_2H_5)CO_2C_2H_5$		Na	(70)	503, 504
		Na	(71)	123

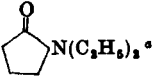
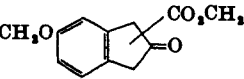
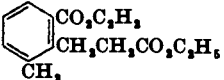
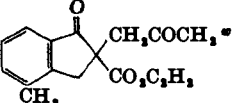
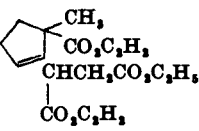
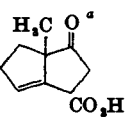
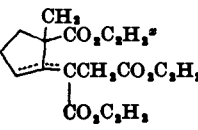
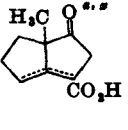
Note: References 231 to 583 are on pp. 197–203.

- ^a This product was isolated after hydrolysis and decarboxylation.
- ^b Alcohol was removed by azeotropic distillation with the solvent.
- ^c Diethyl carbonate was also formed.

TABLE II—Continued
CONDENSATIONS LEADING TO CARBOCYCLIC PRODUCTS

B. Condensations Leading to Five-Membered Rings—Continued

Starting Ester	Product(s)	Base	Yield (%)	Refs.
$C_{10}H_{16}$ (contd.)				
$CH_3CH_2CO_2C_2H_5$ $C(CH_3)_2CO_2C_2H_5$ $CH(C_2H_5)CO_2C_2H_5$		Na	(81)	123
$CH(CH_3)CH_2CO_2C_2H_5$ $CHCO_2C_2H_5$ $CH_2CH_2CH_2CO_2C_2H_5$		Na	(50)	533
$CH_3CH_2CO_2C_2H_5$ $CH_2CHCO_2C_2H_5$ $(CH_3)_2CCO_2C_2H_5$		Na	(52)	527, 530
$CH_3CH_2CO_2C_2H_5$ $CHCO_2C_2H_5$ $CH_2C(C_2H_5)CO_2C_2H_5$		Na	(—)	448
$CH_3CH_2CO_2C_2H_5$ $CHCO_2C_2H_5$ $CH_2C(CH_3OCH_3)CO_2C_2H_5$		Na	(—)	529

$C_{10}H_{11}$ $CH_2CH_2CO_2CH_3$ $CH_2CHCO_2CH_3$ $N(C_2H_5)_2$		Na	(47)	211
$C_{11}H_{13}$ $CH_3O-C_6H_4-CH_2CO_2CH_3$ $CH_2CO_2CH_3$		NaOCH ₃	(27) ^a	467
		Na	(77)	484
$C_{11}H_{14}$ 		Na	(47)	400
		Na	(47)	494

Note: References 231 to 583 are on pp. 197-203.

^a This product was isolated after hydrolysis and decarboxylation.

^r This product was isolated after hydrolysis, decarboxylation, and reesterification.

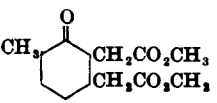
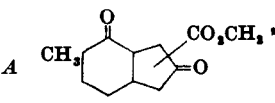
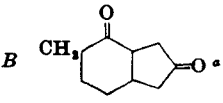
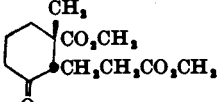
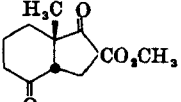
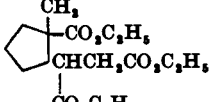
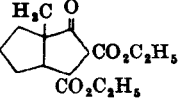
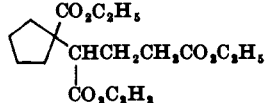
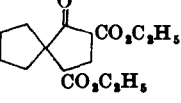
^s The starting material was a mixture of *ortho* and *para* isomers. Both possible esters were produced in yields of 16% and 11%, but identification of the isomers was not accomplished.

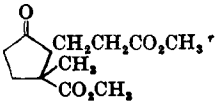
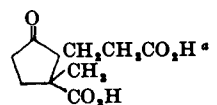
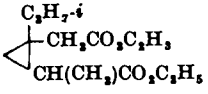
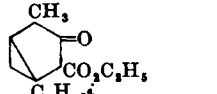
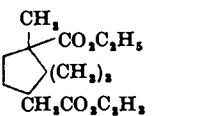
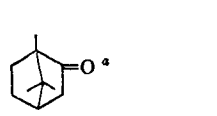
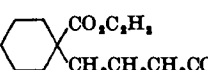
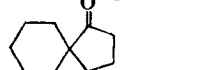
^u The intermediate enolate was alkylated with bromoacetone.

^v The position of the double bond in the starting material and in the product was not established.

TABLE II—Continued
CONDENSATIONS LEADING TO CARBOCYCLIC PRODUCTS

B. Condensations Leading to Five-Membered Rings—Continued

Starting Ester	Product(s)	Base	Yield (%)	Refs.
$C_{11}H_{13}$ 	A 	NaOCH ₃	(A, 43)	498
	B 		(B, —)	403
		NaOCH ₃	(30)	468
		Na	(45)	429, 534
		Na	(52)	505

$\text{CH}(\text{CO}_2\text{CH}_3)\text{CH}_2\text{CH}_2\text{CO}_2\text{CH}_3$ $\text{C}(\text{CH}_3)\text{CO}_2\text{CH}_3$ $\text{CH}_2\text{CH}_2\text{CO}_2\text{CH}_3$		NaOCH_3	(67)	449
$\text{CH}(\text{CO}_2\text{C}_2\text{H}_5)\text{CH}_2\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5$ $\text{C}(\text{CH}_3)\text{CO}_2\text{C}_2\text{H}_5$ $\text{CH}_2\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5$		Na	(91)	126
$\text{C}_{11}\text{H}_{18}$ C_3H_7 		Na	(58)	275
		Na	(68)	41
		NaH	(74)	506

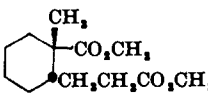
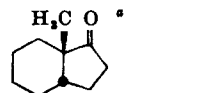
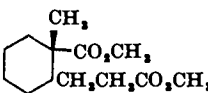
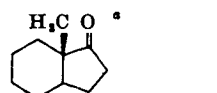
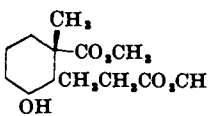
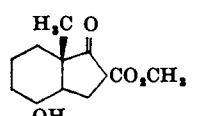
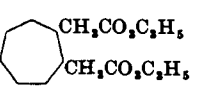
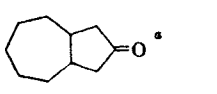
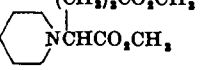
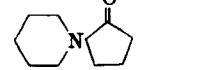
Note: References 231 to 583 are on pp. 197-203.

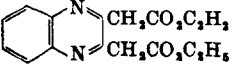
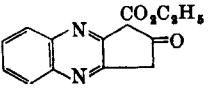
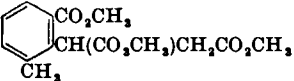
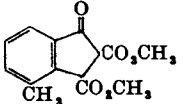
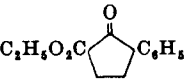
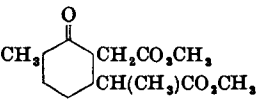
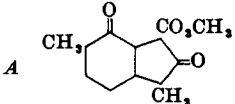
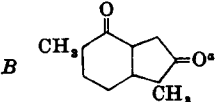
* This product was isolated after hydrolysis and decarboxylation.

* This product was isolated after hydrolysis, decarboxylation, and reesterification.

* The position of the ester group was not established.

TABLE II—Continued
CONDENSATIONS LEADING TO CARBOCYCLIC PRODUCTS

B. Condensations Leading to Five-Membered Rings—Continued				
Starting Ester	Product(s)	Base	Yield (%)	Refs.
$\text{C}_{11}\text{H}_{18}$ (contd.)				
		NaOCH_3	(43)*	270
		NaOCH_3	(53)*	270
		KOC_4H_9	(24)	469
		—	(—)	277
		Na	(52)	211

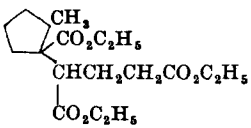
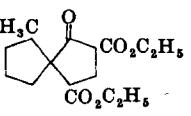
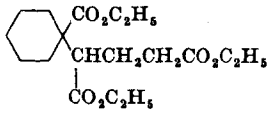
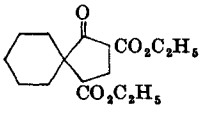
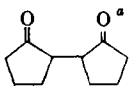
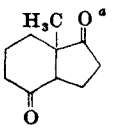
$C_{11}H_{10}-C_{11}H_{11}$			$NaOC_2H_5$	(—)	363
			NaH	(—)	521
$CH(C_2H_5)CO_2C_2H_5$ $CH_2CH_2CH_2CO_2C_2H_5$			$NaOC_2H_5$	(96)	473
$C_{12}H_{18}$			$NaOCH_3$	(A, 24)	498
			—	(B, —)	403

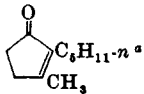
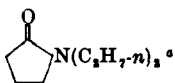
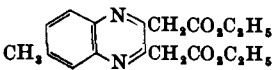
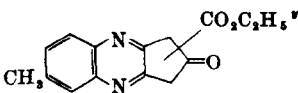
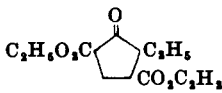
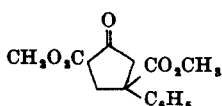
Note: References 231 to 583 are on pp. 197–203.

* This product was isolated after hydrolysis and decarboxylation.

* The yield is based on the starting ester for a series of reactions involving Arndt-Eistert homologation and culminated by the Dieckmann cyclization.

TABLE II—Continued
CONDENSATIONS LEADING TO CARBOCYCLIC PRODUCTS

B. Condensations Leading to Five-Membered Rings—Continued				
Starting Ester	Product(s)	Base	Yield (%)	Refs.
$C_{12}H_{18}$ (contd.)				
		Na	(—)	448
		Na	(48)	389
$CH_2CH_2CH_2CO_2C_2H_5$ $CHCO_2C_2H_5$ $CHCO_2C_2H_5$ $CH_2CH_2CH_2CO_2C_2H_5$		K	(Poor)	269
$CH(CO_2CH_3)CH_2CH_2CO_2CH_3$ $CH_2C(CO_2CH_3)CH_2CH_2CH_2CO_2CH_3$		NaH	(43)	46

$C_{13}H_{20}-C_{13}H_{22}$ $CH_2CH_2CO_2C_2H_5$ $ $ OCH_3 $ $ $C(C_2H_{11-n})CO_2C_2H_5$		Na	(22)	97
$CH_2CH_2CH_2CO_2CH_3$ $ $ $CHN(C_2H_5-n)_2$ $ $ CO_2CH_3		Na	(48)	211
$C_{13}H_{18}-C_{13}H_{20}$ 		NaOC ₂ H ₅	(—)	363
$CH_2CH_2CO_2C_2H_5$ $ $ $CHCO_2C_2H_5$ $ $ $CH(C_2H_5)CO_2C_2H_5$		Na	(69)	444, 442
$CH_2CH_2CO_2CH_3$ $ $ $C(C_2H_5)CO_2CH_3$ $ $ $CH_2CO_2CH_3$		NaOCH ₃	(Quant.)	495

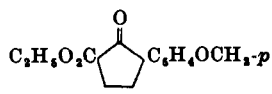
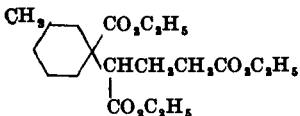
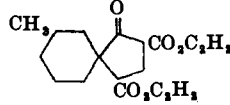
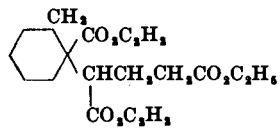
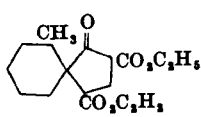
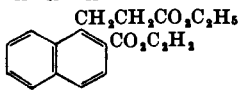
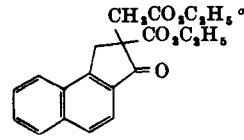
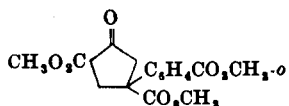
Note: References 231 to 583 are on pp. 197-203.

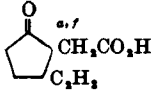
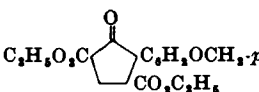
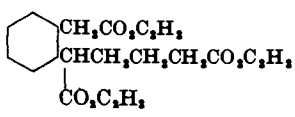
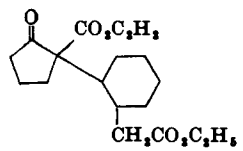
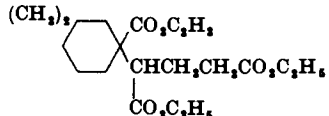
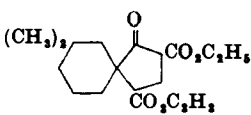
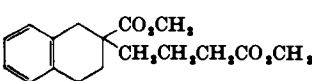
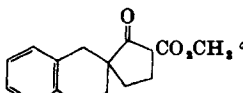
^a This product was isolated after hydrolysis and decarboxylation.

^v The position of the ester group was not established.

TABLE II—Continued
CONDENSATIONS LEADING TO CARBOCYCLIC PRODUCTS

B. Condensations Leading to Five-Membered Rings—Continued

Starting Ester	Product(s)	Base	Yield (%)	Refs.
$C_{13}H_{18}-C_{13}H_{20}$ (contd.) $CH_2CH_2CH_2CO_2C_2H_5$ $ $ $CH(C_2H_5OCH_2-p)CO_2C_2H_5$		NaOC ₂ H ₅ or Na	(50)	475
		Na	(52)	387
		Na	(48)	387
$C_{14}H_{18}-C_{14}H_{20}$ 		Na	(74)	537
$CH_2CH_2CO_2CH_3$ $ $ $C(C_2H_5CO_2CH_2-o)CO_2CH_3$ $ $ $CH_2CO_2CH_3$		NaOCH ₃	(25)	495

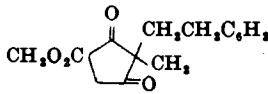
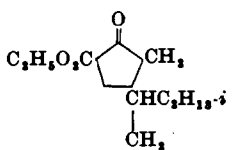
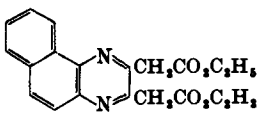
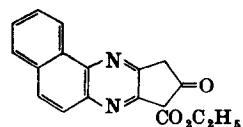
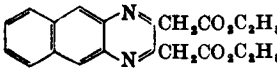
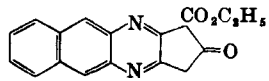
$\text{CH}(\text{CO}_2\text{C}_2\text{H}_5)\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5$ $\text{CH}(\text{C}_6\text{H}_5)\text{CH}_2\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5$ $\text{CH}_2\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5$ $\text{CHCO}_2\text{C}_2\text{H}_5$ $\text{CH}(\text{C}_6\text{H}_5\text{OCH}_2\text{-}p)\text{CO}_2\text{C}_2\text{H}_5$		Na	(Low)	491
$\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5$ $\text{CHCH}_2\text{CH}_2\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5$ $\text{CO}_2\text{C}_2\text{H}_5$		Na	(23)	438, 445
		—	(—)	393
$(\text{CH}_2)_3$ 	$(\text{CH}_2)_3$ 	Na	(—)	448
$\text{C}_{12}\text{H}_{18}\text{-C}_{12}\text{H}_{18}$ 		NaOCH ₃	(92)	408

Note: References 231 to 583 are on pp. 197-203.

- * This product was isolated after hydrolysis and decarboxylation.
- ° Alcohol was removed by azeotropic distillation with the solvent.
- / This product is accompanied by isomeric cyclohexanone; see Table II-C.
- The intermediate enolate was alkylated with ethyl bromoacetate.

TABLE II—Continued
CONDENSATIONS LEADING TO CARBOCYCLIC PRODUCTS

B. Condensations Leading to Five-Membered Rings—Continued

Starting Ester	Product(s)	Base	Yield (%)	Refs.
$\text{C}_{12}\text{H}_{18}\text{-C}_{12}\text{H}_{18}$ (contd.) $\text{COCH}_2\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5$ $\text{C}(\text{CH}_3)\text{CO}_2\text{C}_2\text{H}_5$ $\text{CH}_2\text{CH}_2\text{C}_6\text{H}_5$		Na	(—)	508
$\text{CH}(\text{CH}_3)\text{CO}_2\text{C}_2\text{H}_5$ $\text{CHCH}(\text{CH}_3)\text{C}_6\text{H}_{13}$ $\text{CH}_2\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5$		Na	(67)	539
$\text{C}_{12}\text{H}_{18}\text{-C}_{12}\text{H}_{18}$ 		NaOC ₂ H ₅	(—)	384
		NaOC ₂ H ₅	(—)	384

		NaOCH ₃	(50)	485
C ₁₇ H ₁₈ -C ₁₇ H ₁₈				
		NaOCH ₃	(—)	477
CH ₃ CH ₂ C ₂ H ₄ OCH ₃ - <i>m</i> C(CH ₃)CO ₂ CH ₃ CH(CO ₂ CH ₃)CH ₂ CH ₂ CO ₂ CH ₃ CH(C ₂ H ₅ - <i>i</i>)CO ₂ C ₂ H ₅ C(CH ₃)CO ₂ C ₂ H ₅ CHCO ₂ C ₂ H ₅ CH ₂ CO ₂ C ₂ H ₅		—	(—)	497
C ₁₈ H ₁₈ -C ₁₈ H ₁₈				
		Na	(—)	423
		NaOCH ₃	(63)	496, 398

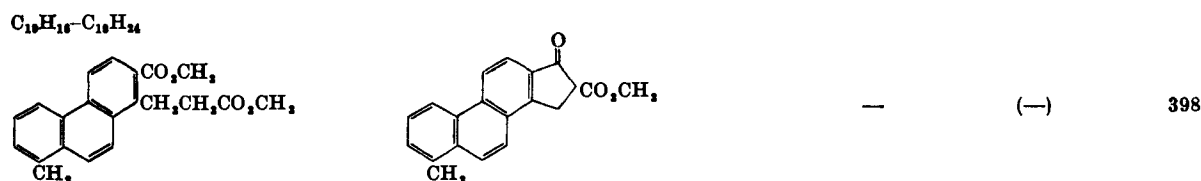
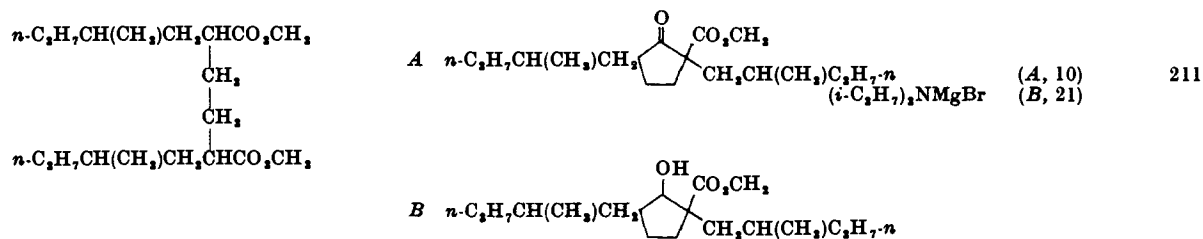
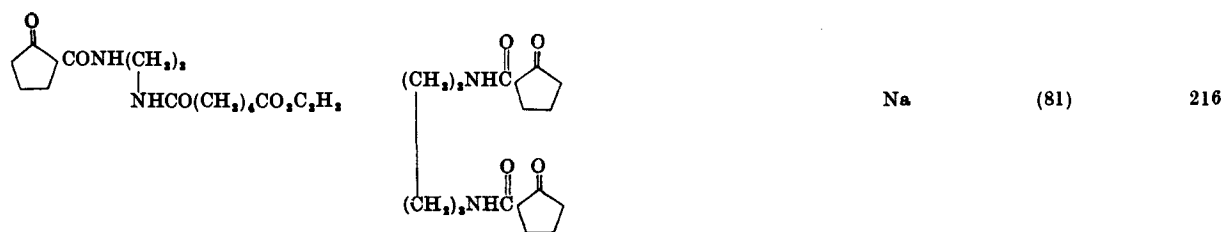
Note: References 231 to 583 are on pp. 197-203.

* This product was isolated after hydrolysis, decarboxylation, and reesterification.

TABLE II—Continued
CONDENSATIONS LEADING TO CARBOCYCLIC PRODUCTS

B. Condensations Leading to Five-Membered Rings—Continued

Starting Ester	Product(s)	Base	Yield (%)	Refs.
C ₁₈ H ₁₈ -C ₁₈ H ₁₈ (cond.)				
		Na	(23)	486
CH(C ₂ H ₅)CH ₂ CO ₂ CH ₃ CH(C ₂ H ₅)CH ₂ CO ₂ CH ₃ (racemic)		Na	(55)	72
CH(C ₂ H ₅)CH ₂ CO ₂ CH ₃ CH(C ₂ H ₅)CH ₂ CO ₂ CH ₃ (meso)		Na	(40)	72
		KOC ₂ H ₅ - <i>t</i>	(19)	435



Note: References 231 to 583 are on pp. 197-203.

* This product was isolated after hydrolysis and decarboxylation.

TABLE II—*Continued*
CONDENSATIONS LEADING TO CARBOCYCLIC PRODUCTS

B. Condensations Leading to Five-Membered Rings—Continued

Starting Ester	Product(s)	Base	Yield (%)	Refs.
$C_{10}H_{18}-C_{19}H_{34}$ (contd.)				
		KOC_4H_9-t	(Quant.)	520
$C_{20}H_{32}-C_{22}H_{36}$				
		$NaOCH_3$ Na	(95-98) (40-50)	222 222
		$NaOCH_3$	(> 75%)	283
$C_{21}H_{34}-C_{21}H_{40}$				
		—	(—)	497

		KOC ₄ H ₉ - <i>t</i>	(37)	309
		KOC ₄ H ₉ - <i>t</i>	(86)	278, 487
		KOC ₄ H ₉ - <i>t</i>	(98)	278
		KOC ₄ H ₉ - <i>t</i> NaH NaOCH ₃	(94) (Poor) (Poor)	273 273 273

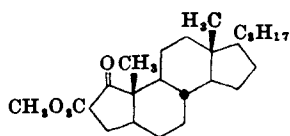
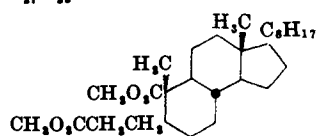
Note: References 231 to 583 are on pp. 197-203.

* This product was isolated after hydrolysis and decarboxylation.

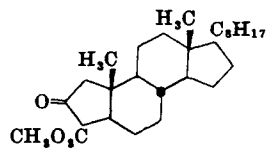
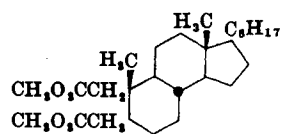
TABLE II—Continued
CONDENSATIONS LEADING TO CARBOCYCLIC PRODUCTS

B. Condensations Leading to Five-Membered Rings—Continued

Starting Ester	Product(s)	Base	Yield (%)	Refs.
<i>C₁₅H₂₅-C₁₅H₂₄ (contd.)</i>				
		KOC ₄ H ₉ - <i>t</i>	(80)	273
<i>C₁₄H₂₃-C₁₄H₂₂</i>				
		KOC ₄ H ₉ - <i>t</i>	(48)	276
		KOC ₄ H ₉ - <i>t</i>	(52)	276
		(<i>i</i> -C ₄ H ₉) ₂ NMgBr	(A, 13) (B, 23)	211

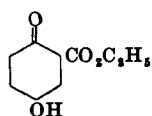
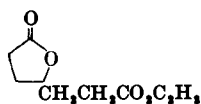
$C_{17}H_{33}$  KOC_4H_9-t (55)

297

 KOC_4H_9-t (80)

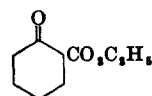
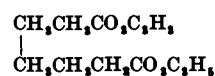
297

C. Condensations Leading to Six-Membered Rings

 $C_7H_{10}-C_7H_{12}$  Na
 $NaOC_4H_9-t$ (7)
(13)

136

136

 Na

(76)

434, 1, 18,
110, 235

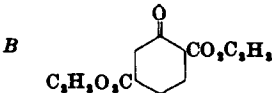
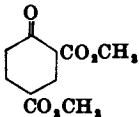
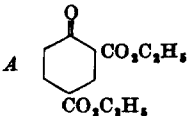
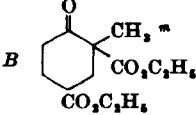
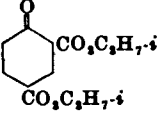
Note: References 231 to 583 are on pp. 197-203.

* This product was isolated after hydrolysis and decarboxylation.

TABLE II—Continued
CONDENSATIONS LEADING TO CARBOCYCLIC PRODUCTS

C. Condensations Leading to Six-Membered Rings—Continued

Starting Ester	Product(s)	Base	Yield (%)	Refs.
C_7H_{10}				
		$NaOC_4H_9$ in C_7H_9OH	(Poor) ^{aa}	120, 121
		$NaOC_4H_9$ in C_7H_9	(50) ^{aa}	121
C_8H_{11}				
		$NaOC_4H_9$	(42)	93
		$NaOCH_3$ Na	(^{bb}) (^{bb})	110 110
		Na	(A, 73)	245, 120, 232, ^{cc} 407

		NaOC_2H_5 in C_2H_5	(A, 50)	121
$\begin{array}{c} \text{CH}_2\text{CH}_2\text{CO}_2\text{CH}_3 \\ \\ \text{CHCO}_2\text{CH}_3 \\ \\ \text{CH}_2\text{CH}_2\text{CO}_2\text{CH}_3 \end{array}$		NaOCH_3 or NaH Na KOC_2H_5	(57-81) (88) (89)	437 547, 440 547
$\begin{array}{c} \text{CH}_2\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5 \\ \\ \text{CHCO}_2\text{C}_2\text{H}_5 \\ \\ \text{CH}_2\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5 \end{array}$		Na	(A, 50)	104
		Na	(B, 91)	547
$\begin{array}{c} \text{CH}_2\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5 \\ \\ \text{CHCO}_2\text{C}_2\text{H}_5 \\ \\ \text{CH}_2\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5 \end{array}$		Na	(75)	221

Note: References 231 to 583 are on pp. 197-203.

^a The intermediate enolate was alkylated with methyl iodide.

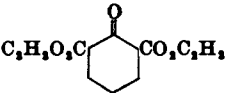
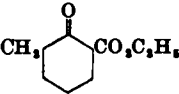
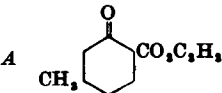
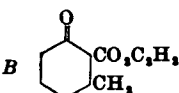
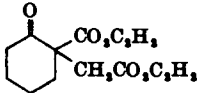
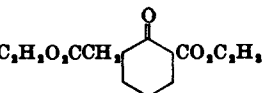
^b This product is accompanied by the isomeric cyclopentanone; see Table II-B.

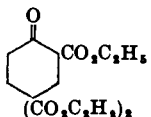
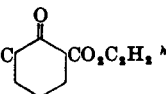
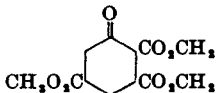
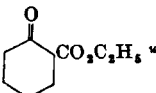
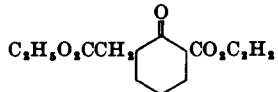
^c With sodium methoxide, A and B together constituted 15% of the reaction mixture, the remainder being the cyclopentanone isomer. With sodium, the mixture contained 18% cyclopentanone and 81% A.

^d This reference describes B as the product, although later workers have found this to be, at best, a minor product.

TABLE II—Continued
CONDENSATIONS LEADING TO CARBOCYCLIC PRODUCTS

C. Condensations Leading to Six-Membered Rings—Continued

Starting Ester	Product(s)	Base	Yield (%)	Refs.
C_2H_{11} (cond.)				
$\begin{array}{c} \text{CH}_2\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5 \\ \\ \text{CH}_2\text{CH}_2\text{CH}(\text{CO}_2\text{C}_2\text{H}_5)_2 \end{array}$		Na	(57)	307
C_2H_{11}				
$\begin{array}{c} \text{CH}_2\text{CH}_2\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5 \\ \\ \text{CH}_2\text{CH}(\text{CH}_3)\text{CO}_2\text{C}_2\text{H}_5 \end{array}$		Na NaH NaOC_2H_5	(70) (90) (54)	306, 42, 287 42 93
$\begin{array}{c} \text{CH}_2\text{CH}_2\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5 \\ \\ \text{CH}(\text{CH}_3)\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5 \end{array}$		Na	(Mostly A)	244
				
C_2H_{11}				
		NaOC_2H_5	(54-63)	522, 418, 419

$\begin{array}{c} \text{CH}_2\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5 \\ \\ \text{C}(\text{CO}_2\text{C}_2\text{H}_5)_2 \\ \\ \text{CH}_2\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5 \end{array}$		Na	(Low)	274
$\begin{array}{c} \text{CH}_2\text{CH}(\text{CO}_2\text{C}_2\text{H}_5)_2 \\ \\ \text{CH}_2\text{CH}_2\text{CH}(\text{CO}_2\text{C}_2\text{H}_5)_2 \end{array}$	$\text{C}_2\text{H}_5\text{O}_2\text{C}$ 	NaOC ₂ H ₅	(25)	27, 28, 29
$\begin{array}{c} \text{CH}(\text{CO}_2\text{CH}_3)\text{CH}_2\text{CO}_2\text{CH}_3 \\ \\ \text{CH}_2\text{CH}(\text{CO}_2\text{CH}_3)\text{CH}_2\text{CO}_2\text{CH}_3 \\ \\ \text{C}_2\text{H}_5 \end{array}$		Na	(30)	379
$\begin{array}{c} \text{CH}_2\text{CH}_2\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5 \\ \\ \text{CH}_2\text{CH}(\text{COCH}_3)\text{CO}_2\text{C}_2\text{H}_5 \end{array}$	<p>A</p>  <p>B</p> $\begin{array}{c} \text{CH}_2\text{CH}_2\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5 \\ \\ \text{CH}_2\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5 \end{array}$	Na NaOC ₂ H ₅ in xylene	(A, 52.5) (A, 56)	320 320
$\begin{array}{c} \text{CH}_2\text{CO}_2\text{C}_2\text{H}_5 \\ \\ \text{CHCO}_2\text{C}_2\text{H}_5 \\ \\ (\text{CH}_2)_4\text{CO}_2\text{C}_2\text{H}_5 \end{array}$		Na	(88)	452, 522

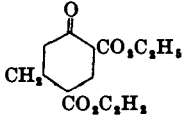
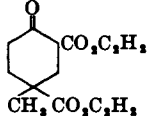
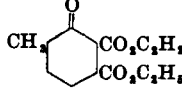
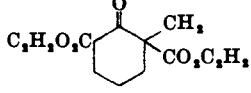
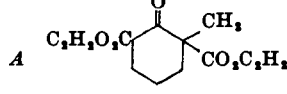
Note: References 231 to 583 are on pp. 197-203.

^a Diethyl carbonate was also formed.

^{*} Ethyl acetate was formed during the reaction.

TABLE II—Continued
CONDENSATIONS LEADING TO CARBOCYCLIC PRODUCTS

C. Condensations Leading to Six-Membered Rings—Continued

Starting Ester	Product(s)	Base	Yield (%)	Refs.
C_2H_{14} (contd.)				
$\begin{array}{c} \text{CH}_2\text{CHCH}_2\text{CO}_2\text{C}_2\text{H}_5 \\ \\ \text{CHCO}_2\text{C}_2\text{H}_5 \\ \\ \text{CH}_2\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5 \end{array}$		Na	(88)	292
$\begin{array}{c} \text{CH}_2\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5 \\ \\ \text{C}(\text{CH}_3)\text{CO}_2\text{C}_2\text{H}_5 \\ \\ \text{CH}_2\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5 \end{array}$		Na	(75)	242
$\begin{array}{c} \text{CH}_2\text{CH}_2\text{CH}(\text{CH}_3)\text{CO}_2\text{C}_2\text{H}_5 \\ \\ \text{CHCO}_2\text{C}_2\text{H}_5 \\ \\ \text{CH}_2\text{CO}_2\text{C}_2\text{H}_5 \end{array}$		Na	(72)	247
$\begin{array}{c} \text{CH}_2\text{CH}_2\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5 \\ \\ \text{CH}_2\text{C}(\text{CO}_2\text{C}_2\text{H}_5)_2\text{CH}_3 \end{array}$		Na	(45)	31
$\begin{array}{c} \text{CH}_2\text{CH}_2\text{CH}(\text{CO}_2\text{C}_2\text{H}_5)_2 \\ \\ \text{CH}_2\text{CH}(\text{CH}_2)\text{CO}_2\text{C}_2\text{H}_5 \end{array}$	<p>A</p> 	1 eq. KOC ₂ H ₅	(A, 45) (B, 4)	31

		1.5 eq. KOC ₂ H ₅	(A, 27) (B, 18)	31 31
		NaOC ₂ H ₅ Na	(A, 54) (A, 15-32) ^{4d} (B, 12-0)	76 136
		Na	(B, —)	137
$C_{10}H_{16}-C_{10}H_{14}$ $CH_2CH_2CO_2C_2H_5$ $ $ $C(CO_2C_2H_5)_2$ $ $ $C=CHCO_2C_2H_5$ $ $ $CO_2C_2H_5$		NaOC ₂ H ₅	(—)	299
		NaOC ₂ H ₅	(70)	346, 418
$CH_2CH(CO_2C_2H_5)CH_2CO_2C_2H_5$ $ $ $CH_2CH(CO_2C_2H_5)CH_2CO_2C_2H_5$		Na	(Good)	262

Note: References 231 to 583 are on pp. 197-203.

^a This product was isolated after hydrolysis and decarboxylation.

^b Diethyl carbonate was also formed.

^{4d} The yield depended on whether a stabilized or freshly prepared sodium dispersion was used. Under the latter conditions the poorer yield was obtained accompanied by 12% of B.

TABLE II—Continued
CONDENSATIONS LEADING TO CARBOCYCLIC PRODUCTS

C. Condensations Leading to Six-Membered Rings—Continued

Starting Ester	Product(s)	Base	Yield (%)	Refs.
$C_{10}H_{16}-C_{10}H_{14}$ (contd.) $CH(CO_2C_2H_5)CH_2CO_2C_2H_5$ $ $ $C(CH_3)CO_2C_2H_5$ $ $ $CH_2CH_2CO_2C_2H_5$		Na	(60)	126
$CH_2CH_2CH(CO_2C_2H_5)_2$ $ $ $CH(CH_3)CH(CO_2C_2H_5)_2$		NaOC ₂ H ₅	(35)	32
$C_{10}H_{16}$ $CH_2CH_2CO_2C_2H_5$ $ $ $C=C(CH_3)_2$ $ $ $CH_2CH_2CO_2C_2H_5$		Na	(—)	460
		Na	(30)	124, 125

$\begin{array}{c} \text{CH}_3\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5 \\ \\ \text{CH}_2\text{CH}_2\text{C}(\text{CH}_3)\text{CO}_2\text{C}_2\text{H}_5 \\ \\ \text{CH}_2\text{CO}_2\text{C}_2\text{H}_5 \end{array}$		Na	(—)	532b
$\begin{array}{c} \text{CH}_2\text{CO}_2\text{C}_2\text{H}_5 \\ \\ \text{C}(\text{CH}_3)\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5 \\ \\ \text{CH}_2\text{CH}_2\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5 \end{array}$		Na	(75)	102
$\begin{array}{c} \text{CH}_3\text{CH}(\text{CH}_3)\text{CO}_2\text{C}_2\text{H}_5 \\ \\ \text{CHCO}_2\text{C}_2\text{H}_5 \\ \\ \text{CH}(\text{CH}_3)\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5 \end{array}$		Na	(51-83)	292
$\begin{array}{c} \text{CH}(\text{CH}_3)\text{CH}(\text{CH}_3)\text{CO}_2\text{C}_2\text{H}_5 \\ \\ \text{CHCO}_2\text{C}_2\text{H}_5 \\ \\ \text{CH}_2\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5 \end{array}$		Na	(85)	292
$\begin{array}{c} \text{C}(\text{CH}_3)_2\text{CO}_2\text{C}_2\text{H}_5 \\ \\ \text{CHCO}_2\text{C}_2\text{H}_5 \\ \\ \text{CH}_2\text{CH}_2\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5 \end{array}$		Na	(88)	355

Note: References 231 to 583 are on pp. 197-203.

* This product was isolated after hydrolysis and decarboxylation.

^a Diethyl carbonate was also formed.

¹ This is the most probable structure; ¹¹², ¹²² see text, pp. 21-22.

² This product was isolated after hydrolysis, decarboxylation, and reesterification.

TABLE II—Continued
CONDENSATIONS LEADING TO CARBOCYCLIC PRODUCTS

C. Condensations Leading to Six-Membered Rings—Continued

Starting Ester	Product(s)	Base	Yield (%)	Refs.
$\text{C}_{10}\text{H}_{18}$ (contd.)				
$\begin{array}{c} \text{CH}_3\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5 \\ \\ \text{CHCO}_2\text{C}_2\text{H}_5 \\ \\ \text{CH}_2\text{C}(\text{CH}_3)_2\text{CO}_2\text{C}_2\text{H}_5 \end{array}$		Na	(—)	392
$\begin{array}{c} \text{CH}_3\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5 \\ \\ \text{CHCO}_2\text{C}_2\text{H}_5 \\ \\ \text{C}(\text{CH}_3)_2\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5 \end{array}$		Na	(70)	527, 530
$\begin{array}{c} \text{CH}_3\text{CH}(\text{CH}_3)\text{CO}_2\text{CH}_3 \\ \\ \text{CH}_2\text{C}(\text{CH}_3)_2\text{CH}_2\text{CO}_2\text{CH}_3 \\ \\ \text{CO}_2\text{CH}_3 \end{array}$		Na NaOCH ₃	(64-78) (0)	119, 531 119
$\text{C}_{10}\text{H}_{18}$				
$\begin{array}{c} \text{CH}(\text{CH}_2\text{SC}_2\text{H}_5)\text{CO}_2\text{C}_2\text{H}_5 \\ \\ \text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5 \end{array}$		Na	(42)	523

$C_{11}H_{18}-C_{11}H_{18}$

		NaOCH ₃	(70)	254
		Na	(—)	114
$CH_2CH(CO_2CH_3)_2$ $C(CO_2CH_3)_2$ $CH_2CH(CO_2CH_3)_2$		Na	(A, 50)	92
			(B, 14)	92
			(0)	146

Note: References 231 to 583 are on pp. 197-203.

* This product was isolated after hydrolysis and decarboxylation.

* Various Dieckmann conditions were tried without success.

TABLE II—Continued
CONDENSATIONS LEADING TO CARBOCYCLIC PRODUCTS

C. Condensations Leading to Six-Membered Rings—Continued

Starting Ester	Product(s)	Base	Yield (%)	Refs.
$C_{11}H_{18}$ 		NaH	(21)	426
$CH(CO_2C_2H_5)CH_2CH_2CO_2C_2H_5$ CH_2 $CH(CO_2C_2H_5)CH_2CH_2CO_2C_2H_5$		K	(50)	45
$CH_2CHCH_2CO_2C_2H_5$ $CHCO_2C_2H_5$ $CH_2C(CH_3)(CO_2C_2H_5)_2$		Na	(88)	292
$C_{11}H_{18}$ 		Na	(53)	483
		Na	(—)	268

		—	(—)	238
		NaOC2H5	(—)	342
		NaOC2H5	(—)	342
		Na	(A + B, —)	396
		Na	(—)	397

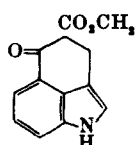
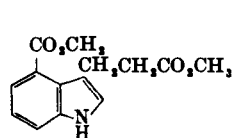
Note: References 231 to 583 are on pp. 197–203.

* This product was isolated after hydrolysis and decarboxylation.

TABLE II—Continued
CONDENSATIONS LEADING TO CARBOCYCLIC PRODUCTS

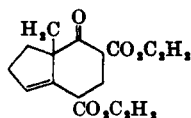
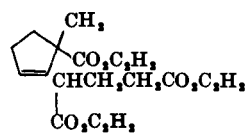
C. Condensations Leading to Six-Membered Rings—Continued

Starting Ester	Product(s)	Base	Yield (%)	Refs.
$C_{11}H_{20}$ 		NaOC2H5	(40)	340
		Na	(Quant.)	378
$C_{12}H_{20}$ – $C_{13}H_{22}$ 		NaH**	(75)	149
		NaH	(86)	149

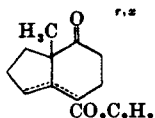
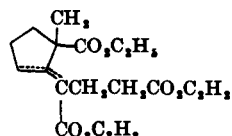


(0) 148

C₁₁H₁₈

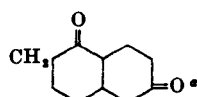
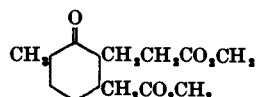


Na (—) 400



Na (33) 494

C₁₁H₁₈



Na (31) 457

Note: References 231 to 583 are on pp. 197-203.

- * This product was isolated after hydrolysis and decarboxylation.
- * This product was isolated after hydrolysis, decarboxylation, and reesterification.
- * Various Dieckmann conditions were tried without success.
- * The position of the double bond in the starting material and in the product was not established.
- ** The reaction was carried out in tetrahydrofuran. In ether, no cyclization was observed.

THE DIECKMANN CONDENSATION

97

TABLE II—Continued
CONDENSATIONS LEADING TO CARBOCYCLIC PRODUCTS

98

C. Condensations Leading to Six-Membered Rings—Continued

Starting Ester	Product(s)	Base	Yield (%)	Refs.
C ₁₁ H ₁₈ (contd.)				
		Na	(—)	535
		NaH	(43)	46
		Na	(69)	454
C ₁₂ H ₂₀				
		Na	(60)	439

ORGANIC REACTIONS

		Na	(51)	536
		NaOCH ₃	(90)	430, 431
C ₁₁ H ₁₁ 	—		(0)	147
C ₁₁ H ₁₄ -C ₁₁ H ₁₆ 		Na	(—)	453
		NaOCH ₃	(90)	433

Note: References 231 to 583 are on pp. 197-203.

- * This product was isolated after hydrolysis and decarboxylation.
 † Alcohol was removed by azeotropic distillation with the solvent.
 ‡ Various Dieckmann conditions were tried without success.
 § The position of the ester group was not established.

TABLE II—Continued
CONDENSATIONS LEADING TO CARBOCYCLIC PRODUCTS

C. Condensations Leading to Six-Membered Rings—Continued

Starting Ester	Product(s)	Base	Yield (%)	Refs.
C ₁₁ H ₁₄ -C ₁₁ H ₁₆ (contd.)				
		Na	(—)	367
		NaOC ₂ H ₅	(33)	361
		— NaH NaOCH ₃ Na	(—) (63) (35) (30)	405 457 457 457
		NaH	(A, 56) " (B, 44)	110 110
		KOC ₂ H ₅ -t	(A, 42) " (B, 58)	110 110
		NaOC ₂ H ₅	(A, 38) " (B, 62)	110 110

$C_{14}H_{14}$ 		Na	(0)	148
$C_{14}H_{14}$ 		NaOCH3 NaH	(49) (38)	458 458
$CH_3CH_2CH_2CO_2C_2H_5$ $CH_2CH(COC_2H_5)CO_2C_2H_5$		Na	(55)	320
$CH_3CH_2CO_2CH_3$ $C(C_2H_5)CO_2CH_3$ $CH_3CH_2CO_2CH_3$		NaOCH3	(98)	495
$CH_3CH_2CO_2C_2H_5$ $C(C_2H_5)CO_2C_2H_5$ $CH_3CH_2CO_2C_2H_5$		Na	(65)	243

Note: References 231 to 583 are on pp. 197-203.

* This product was isolated after hydrolysis and decarboxylation.

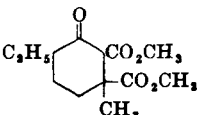
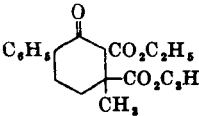
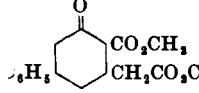
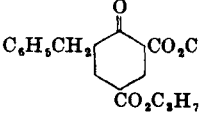
** These are relative yields of A and B, not the overall yield.

*** Ethyl benzoate is also produced during the reaction.

TABLE II—Continued
CONDENSATIONS LEADING TO CARBOCYCLIC PRODUCTS

C. Condensations Leading to Six-Membered Rings—Continued

Starting Ester	Product(s)	Base	Yield (%)	Refs.
$C_{14}H_{14}$ (contd.)				
$CH(CO_2CH_3)CH_2CO_2CH_3$ $CH(C_2H_5)CH_2CH_2CO_2CH_3$		Na	(—)	491
$CH_3CH_2CH_2CO_2C_2H_5$ $CHCO_2C_2H_5$ $CH(C_2H_5)CO_2C_2H_5$		Na	(—)	442
$C_{14}H_{14}$ — $C_{14}H_{14}$ $CH_3CH_2CH_2CO_2CH_3$ $CHC_2H_5OCH_3$ $CH_3CO_2CH_3$		Na	(—)	538
$CH_3CO_2C_2H_5$ 		—	(—)	393
$C_{14}H_{14}$ 		Na	(—)	507

$C_{11}H_{14}$ $CH_2CH_2CH(C_2H_5)CO_2CH_3$ $ $ $C(CH_3)CO_2CH_3$ $ $ $CH_2CO_2CH_3$		Na	(—)	531
$CH_2CH_2CH(C_2H_5)CO_2C_2H_5$ $ $ $C(CH_3)CO_2C_2H_5$ $ $ $CH_2CO_2C_2H_5$		Na	(42)	116, 509, 510
$CH_2CH(C_2H_5)CH_2CO_2CH_3$ $ $ $CHCH_2CO_2CH_3$ $ $ $CH_2CO_2CH_3$		Na	(74)	339
$CH_2CH_2CO_2C_2H_5$ $ $ $CHCO_2C_2H_5$ $ $ $CH_2CH(CH_2C_2H_5)CO_2C_2H_5$		Na	(45)	221

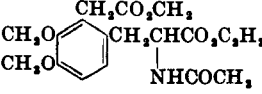
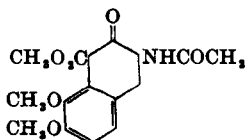
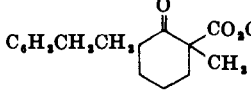
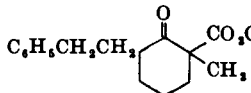
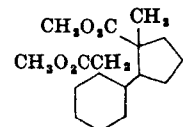
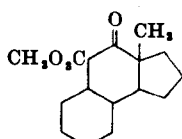
Note: References 231 to 583 are on pp. 197-203.

* This product was isolated after hydrolysis and decarboxylation.

** This product is accompanied by the isomeric cyclopentanone, see Table II-B.

TABLE II—Continued
CONDENSATIONS LEADING TO CARBOCYCLIC PRODUCTS

C. Condensations Leading to Six-Membered Rings—Continued

Starting Ester	Product(s)	Base	Yield (%)	Refs.
$C_{11}H_{14}-C_{10}H_{10}$ 		NaOCH ₃	(33)	482
$CH_2CH_2C_2H_5$ $ $ $CHCO_2CH_3$ $ $ $(CH_3)_4CO_2CH_3$		Na	(Low)	450
$CH_2CH_2C_2H_5$ $ $ $CHCO_2C_2H_5$ $ $ $(CH_3)_4CO_2C_2H_5$		Na	(28)	450
$C_{12}H_{14}$ 		—	(—)	393

$C_{16}H_{14}$ 		Na	(Good)	537
$C_{16}H_{16}$ 		Na	(A, —)	541
		Na	(B, —)	461
		Na	(A, —)	459
		Na	(B, 53)	459

Note: References 231 to 583 are on pp. 197–203.

^a This product was isolated after hydrolysis and decarboxylation.

^m The intermediate enolate was alkylated with methyl iodide.

ⁿ The intermediate enolate was alkylated with ethyl iodide.

TABLE II—Continued
CONDENSATIONS LEADING TO CARBOCYCLIC PRODUCTS

C. Condensations Leading to Six-Membered Rings—Continued

Starting Ester	Product(s)	Base	Yield (%)	Refs.
$C_{16}H_{18}$ 		Na	(66)	541
		NaOCH ₃	(85)	283
		NaOCH ₃	(80)	408
$C_{16}H_{20}$ 		NaOCH ₃	(64)	408
		NaOCH ₃	(78)	408

$\begin{array}{c} \text{(CH}_2\text{)}_3\text{CO}_2\text{CH}_3 \\ \\ \text{CH}_3\text{O} \text{---} \text{C}_6\text{H}_4 \text{---} \text{C}_6\text{H}_4 \text{---} \text{CO}_2\text{CH}_3 \end{array}$	$\begin{array}{c} \text{CH}_3\text{O} \text{---} \text{C}_6\text{H}_4 \text{---} \text{C}_6\text{H}_4 \text{---} \text{C(=O)CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CO}_2\text{CH}_3 \end{array}$	NaH + NaOCH ₃	(32)	271
$\begin{array}{c} \text{CH}_3\text{CH}_2\text{CH}_2\text{CO}_2\text{CH}_3 \\ \\ \text{CHC}_6\text{H}_4\text{OCH}_3 \text{---} p \\ \\ \text{CH(CO}_2\text{CH}_3\text{)CH}_2\text{CO}_2\text{CH}_3 \end{array}$	$\begin{array}{c} \text{CH}_3\text{O}_2\text{CCH}_2\text{C(=O)CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CO}_2\text{CH}_3 \\ \\ p\text{-CH}_2\text{OC}_6\text{H}_4 \end{array}$	NaOCH ₃	(25)	432
$\begin{array}{c} \text{CH}_3\text{CO}_2\text{C}_2\text{H}_5 \\ \\ \text{C(CH}_2\text{)}_2\text{CO}_2\text{C}_2\text{H}_5 \\ \\ \text{CH}_2\text{CH}_2\text{CHCO}_2\text{C}_2\text{H}_5 \\ \\ \text{C}_6\text{H}_4\text{OCH}_3 \text{---} p \end{array}$	$\begin{array}{c} \text{O} \\ \\ p\text{-CH}_2\text{OC}_6\text{H}_4 \text{---} \text{C}_6\text{H}_4 \text{---} \text{C(=O)CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5 \\ \\ \text{CH}_3 \end{array}$	Na	(—)	492, 532a
$\begin{array}{c} \text{C}_6\text{H}_4\text{OCH}_3 \text{---} p \\ \\ \text{CHCH}_2\text{CH}_2\text{CH}_2\text{CO}_2\text{CH}_3 \\ \\ \text{CH(CO}_2\text{CH}_3\text{)CH}_2\text{CO}_2\text{CH}_3 \end{array}$	$\begin{array}{c} \text{CH}_3 \\ \\ \text{CH}_3\text{O}_2\text{C} \text{---} \text{C(=O)CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CO}_2\text{CH}_3 \\ \\ \text{C}_6\text{H}_4\text{OCH}_3 \text{---} p \end{array}$	NaH	(A, 43) (B, 29)	272, 279
	$\begin{array}{c} \text{CH}_3\text{O}_2\text{C} \text{---} \text{C(=O)CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CO}_2\text{CH}_3 \\ \\ \text{CH}_3 \end{array}$			
	$\begin{array}{c} \text{CH}_3\text{O}_2\text{C} \text{---} \text{C(=O)CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CO}_2\text{CH}_3 \\ \\ \text{CH}_3 \end{array}$			

Note: References 231 to 583 are on pp. 197–203.

^a This product was isolated after hydrolysis and decarboxylation.

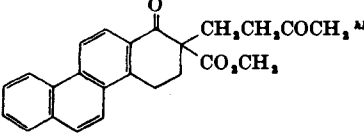
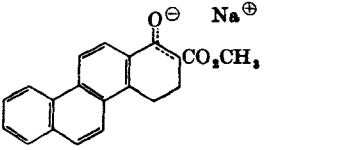
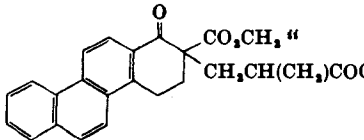
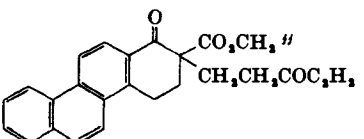
^c Alcohol was removed by azeotropic distillation with the solvent.

^m The intermediate enolate was alkylated with methyl iodide.

TABLE II—Continued
CONDENSATIONS LEADING TO CARBOCYCLIC PRODUCTS

C. Condensations Leading to Six-Membered Rings—Continued

Starting Ester	Product(s)	Base	Yield (%)	Refs.
$\begin{array}{c} \text{CH}_3 \\ \\ \text{CH}_2\text{CHCH}_2\text{CO}_2\text{C}_2\text{H}_5 \\ \\ \text{CO}_2\text{C}_2\text{H}_5 \\ \\ \text{CH}_3 \end{array}$	$\begin{array}{c} \text{CH}_3 \\ \\ \text{CH}_2\text{CHCH}_2\text{CO}_2\text{C}_2\text{H}_5 \\ \\ \text{CO}_2\text{C}_2\text{H}_5 \\ \\ \text{CH}_3 \end{array}$	Na	(A, —)	459
$\begin{array}{c} \text{CH}_3 \\ \\ \text{CH}_2\text{CHCH}_2\text{CO}_2\text{C}_2\text{H}_5 \\ \\ \text{CO}_2\text{C}_2\text{H}_5 \\ \\ \text{CH}_3 \end{array}$	$\begin{array}{c} \text{CH}_3 \\ \\ \text{CH}_2\text{CHCH}_2\text{CO}_2\text{C}_2\text{H}_5 \\ \\ \text{CO}_2\text{C}_2\text{H}_5 \\ \\ \text{CH}_3 \end{array}$	Na	(B, —)	459
$\begin{array}{c} \text{CH}_3\text{O} \text{---} \text{C}_6\text{H}_4 \text{---} \text{C}_6\text{H}_4 \text{---} \text{C(=O)CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CO}_2\text{CH}_3 \end{array}$	$\begin{array}{c} \text{CH}_3\text{O} \text{---} \text{C}_6\text{H}_4 \text{---} \text{C}_6\text{H}_4 \text{---} \text{C(=O)CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CO}_2\text{CH}_3 \end{array}$	Na	(36)	540
$\begin{array}{c} \text{C}_6\text{H}_4\text{OCH}_3 \text{---} p \\ \\ \text{CHCH}_2\text{CH}_2\text{CH}_2\text{CO}_2\text{CH}_3 \\ \\ \text{CH(CO}_2\text{CH}_3\text{)CH}_2\text{CO}_2\text{CH}_3 \end{array}$	$\begin{array}{c} \text{CH}_3 \\ \\ \text{CH}_3\text{O}_2\text{C} \text{---} \text{C(=O)CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CO}_2\text{CH}_3 \\ \\ \text{C}_6\text{H}_4\text{OCH}_3 \text{---} p \end{array}$	NaOCH ₃	(A, 60)	463

<i>B</i>		NaOCH_3	(<i>B</i> , 60)	463
<i>C</i>		Na	(<i>C</i> , —)	128
<i>D</i>		K	(<i>D</i> , 55)	128
<i>E</i>		Na	(<i>E</i> , 75)	128

Note: References 231 to 583 are on pp. 197–203.

^a This product was isolated after hydrolysis and decarboxylation.

^b The intermediate enolate was alkylated with methyl iodide.

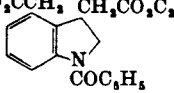
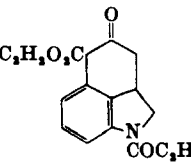
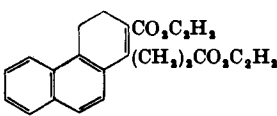
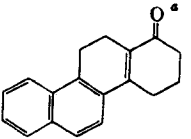
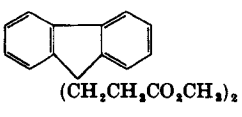
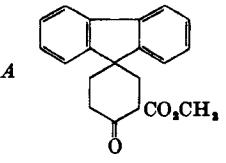
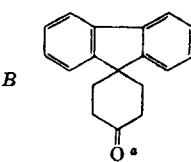
^{aa} The intermediate enolate was alkylated with 4-piperidinobutan-2-one methiodide.

[“] The intermediate enolate was alkylated with 3-methyl-4-piperidinobutan-2-one methiodide.

[“] The intermediate enolate was alkylated with 1-chloropentan-3-one.

TABLE II—Continued
CONDENSATIONS LEADING TO CARBOCYCLIC PRODUCTS

C. Condensations Leading to Six-Membered Rings—Continued

Starting Ester	Product(s)	Base	Yield (%)	Refs.
$\text{C}_{11}\text{H}_{16}-\text{C}_{11}\text{H}_{17}$ (contd.)				
$\text{C}_2\text{H}_5\text{O}_2\text{CCH}_2\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5$ 	$\text{C}_2\text{H}_5\text{O}_2\text{C}$ 	NaH	(95)	149
$\text{C}_{11}\text{H}_{18}$ 		Na	(—)	463
 $(\text{CH}_2\text{CH}_2\text{CO}_2\text{CH}_3)_2$	<i>A</i> 	NaOCH_3	(<i>A</i> , 90)	511
	<i>B</i> 	Na-K	(<i>B</i> , 18)	160

		Na-K NaH	(23) (0)	160 160
$C_{18}H_{20}-C_{18}H_{24}$				
		Na	(—)	462
		NaOCH ₃	(43)	443
		Na	(17)	140

Note: References 231 to 583 are on pp. 197-203.

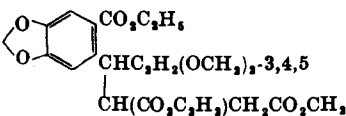
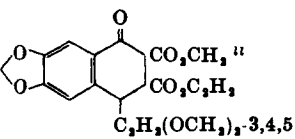
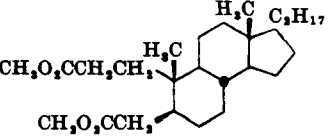
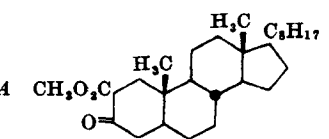
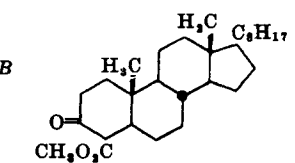
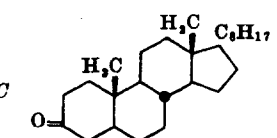
^a This product was isolated after hydrolysis and decarboxylation.

^{kk} Dehydration and decarboxylation occurred before isolation. Some β -ketonic ester was also obtained but was not characterized.

TABLE II—Continued
CONDENSATIONS LEADING TO CARBOCYCLIC PRODUCTS

C. Condensations Leading to Six-Membered Rings—Continued

Starting Ester	Product(s)	Base	Yield (%)	Refs.
$C_{20}H_{18}-C_{20}H_{22}$				
	A	Na	(A, 58-68)	128
	B	Na	(B, 55)	128
		NaOCH ₃	(65)	463
		NaOCH ₃	(53)	428

$C_{12}H_{22}$ 		Na-K NaOCH ₃	(11) (20)	572 571
$C_{28}H_{48}$ 	A 	Na	(A, 52)	139
	B 		(B, 20)	139
	C 		(C, 2)	139

Note: References 231 to 583 are on pp. 197-203.

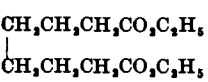
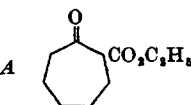
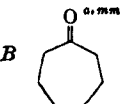
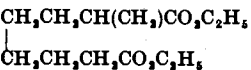
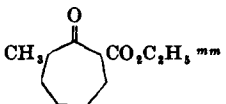
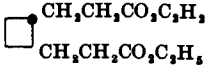
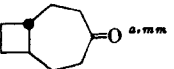
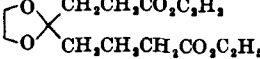
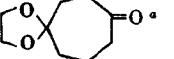
* This product was isolated after hydrolysis and decarboxylation.

** The intermediate enolate was alkylated with 4-piperidinobutan-2-one methiodide.

"" The intermediate enolate was alkylated with 1-chloropentan-3-one.

"" The relative positions of the carbomethoxy and carbethoxy groups were not established.

TABLE II—Continued
CONDENSATIONS LEADING TO CARBOCYCLIC PRODUCTS

D. Condensations Leading to Seven-Membered Rings				
Starting Ester	Product(s)	Base	Yield (%)	Refs.
C_8H_{14} 	A 	Na KOC ₂ H ₅ -t NaH	(A, —) (B, 47) (47-58)	16 49 212
	B 			
$C_{10}H_{18}$ 		KOC ₂ H ₅ -t	(72)	466
$C_{10}H_{18}$ 		NaH	(51)	47
		NaH	(39)	137

$C_{16}H_{18}$ $\begin{array}{c} \text{CH}(\text{OCH}_3)\text{CH}_2\text{CH}_2\text{CO}_2\text{CH}_3 \\ \\ \text{CH}(\text{OCH}_3)\text{CH}_2\text{CH}_2\text{CO}_2\text{CH}_3 \end{array}$		Na	(31)	138
$C_{12}H_{14}-C_{12}H_{20}$ $\begin{array}{c} \text{CH}_2\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5 \\ \\ \text{CH}_2\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5 \end{array}$		Na	(2-3)	254
$C_{14}H_{20}$ $\begin{array}{c} \text{O} \\ \\ (\text{CH}_2)_3\text{C}-\text{CH}_2\text{CH}_2\text{CH}(\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5) \end{array}$		KOC_4H_9-t	(71)	214
$C_{14}H_{20}$ $\begin{array}{c} \text{CH}_2\text{O} \\ \\ \text{CH}_2\text{O} \end{array} \text{C}_6\text{H}_4 \begin{array}{c} \text{CH}_2\text{CH}_2\text{CH}_2\text{CO}_2\text{CH}_3 \\ \\ \text{CH}_2\text{CO}_2\text{CH}_3 \end{array}$		Na	(64)	140, 48
$C_{16}H_{18}-C_{16}H_{20}$ $\begin{array}{c} \text{CH}_2\text{CO}_2\text{C}_2\text{H}_5 \\ \\ \text{CH}_2\text{CO}_2\text{C}_2\text{H}_5 \end{array}$		Na	(80)	344

Note: References 231 to 583 are on pp. 197-203.

* This product was isolated after hydrolysis and decarboxylation.

• Alcohol was removed by azeotropic distillation with the solvent.

^{mm} The reaction was conducted under high-dilution conditions.

TABLE II—Continued
CONDENSATIONS LEADING TO CARBOCYCLIC PRODUCTS

D. Condensations Leading to Seven-Membered Rings—Continued

Starting Esters	Product(s)	Base	Yield (%)	Refs.
$C_{16}H_{18}-C_{16}H_{22}$ (contd.)				
		Na	(33)	540
$\begin{array}{c} \text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CO}_2 \\ \\ \text{CH}_2\text{O} \end{array} \text{C}_6\text{H}_4 \begin{array}{c} \text{CH}_2\text{CO}_2\text{CH}_3 \\ \\ \text{CH}_2\text{CO}_2\text{CH}_3 \end{array}$		$\text{NaH} + \text{NaOCH}_3$	(44)	271
$C_{14}H_{20}$ $\begin{array}{c} \text{O} \\ \\ (\text{CH}_2)_3\text{C}-\text{CH}_2\text{CH}_2\text{CH}(\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5) \end{array}$		KOC_4H_9-t	(63)	214
$C_{18}H_{24}$ $\begin{array}{c} \text{CH}_2\text{O} \\ \\ \text{CH}_2\text{O} \end{array} \text{C}_6\text{H}_4 \begin{array}{c} \text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CO}_2\text{CH}_3 \\ \\ \text{CH}_2\text{CO}_2\text{CH}_3 \end{array}$		K	(20)	540

E. Condensations Leading to Eight-Membered and Larger Rings

$\begin{array}{c} \text{CH}_3\text{CH}_2\text{CH}_2\text{CO}_2\text{CH}_3 \\ \\ \text{CH}_3 \\ \\ \text{CH}_3\text{CH}_2\text{CH}_2\text{CO}_2\text{CH}_3 \end{array}$		NaH	(47)	50
$\begin{array}{c} \text{CH}_3\text{CH}_2\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5 \\ \\ \text{CH}_3 \\ \\ \text{CH}_3\text{CH}_2\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5 \end{array}$	$(\text{CH}_2)_7 \text{ CO } \text{d.c., mm., nn.}$	KOC ₂ H ₅ -t	(15)	49
$\begin{array}{c} \text{CH}_3\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5 \\ \\ (\text{CH}_2)_3 \\ \\ \text{CH}_3\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5 \end{array}$	$(\text{CH}_2)_{10} \text{ CO } \text{d.c., mm., nn.}$	KOC ₄ H ₉ -t	(0.5)	49
$\begin{array}{c} \text{CH}_3\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5 \\ \\ (\text{CH}_2)_7 \\ \\ \text{CH}_3\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5 \end{array}$	$(\text{CH}_2)_{11} \text{ CO } \text{d.c., mm., nn.}$	KOC ₂ H ₅ -t	(0.5)	49
$\begin{array}{c} \text{CH}_3\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5 \\ \\ (\text{CH}_2)_{11} \\ \\ \text{CH}_3\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5 \end{array}$	$(\text{CH}_2)_{13} \text{ CO } \text{d.c., mm., nn.}$	KOC ₄ H ₉ -t	(24)	49

Note: References 231 to 583 are on pp. 197-203.

^a This product was isolated after hydrolysis and decarboxylation.

^b Alcohol was removed by azeotropic distillation with the solvent.

^{mm} The reaction was conducted under high-dilution conditions.

ⁿⁿ The dimeric ketone was also obtained; see below.

TABLE II—Continued
CONDENSATIONS LEADING TO CARBOCYCLIC PRODUCTS

E. Condensations Leading to Eight-Membered and Larger Rings—Continued

Starting Ester	Product(s)	Base	Yield (%)	Refs.
$\begin{array}{c} \text{CH}_3\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5 \\ \\ (\text{CH}_2)_3 \\ \\ \text{CH}_3\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5 \end{array}$	$(\text{CH}_2)_{13} \text{ CO } \text{d.c., mm., nn.}$	KOC ₄ H ₉ -t	(32)	49
$\begin{array}{c} \text{CH}_3\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5 \\ \\ (\text{CH}_2)_{10} \\ \\ \text{CH}_3\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5 \end{array}$	$(\text{CH}_2)_{14} \text{ CO } \text{d.c., mm., nn.}$	KOC ₄ H ₉ -t	(48)	49
$\begin{array}{c} \text{CH}_3\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5 \\ \\ (\text{CH}_2)_3 \\ \\ \text{CH}_3\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5 \end{array}$		KOC ₄ H ₉ -t	(11)	49
$\begin{array}{c} (\text{CH}_2)_3\text{CO}_2\text{CH}_3 \\ \\ \text{C}_6\text{H}_5 \\ \\ (\text{CH}_2)_3\text{CO}_2\text{CH}_3 \end{array}$	$(\text{CH}_2)_3\text{CH}_2 \text{ CO } \text{d.c., mm., nn.}$	KOC ₄ H ₉ -t	(37)	51
$\begin{array}{c} \text{CH}_3\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5 \\ \\ (\text{CH}_2)_4 \\ \\ \text{CH}_3\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5 \end{array}$		KOC ₄ H ₉ -t	(28)	49

$\begin{array}{c} (\text{CH}_2)_7\text{CO}_2\text{CH}_3 \\ \\ \text{C}_6\text{H}_5 \\ \\ (\text{CH}_2)_7\text{CO}_2\text{CH}_3 \end{array}$	$\begin{array}{c} (\text{CH}_2)_6\text{CH}_3 \text{ a.c., mm., mm} \\ \\ \text{C}_6\text{H}_5 \\ \\ (\text{CH}_2)_6\text{CH}_3 \\ \\ \text{CO} \end{array}$	KOC ₄ H ₉ -t	(12)	51
$\begin{array}{c} \text{CH}_3\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5 \\ \\ (\text{CH}_2)_8 \\ \\ \text{CH}_3\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5 \end{array}$	$\begin{array}{c} (\text{CH}_2)_8 \\ \\ \text{OC} \quad \text{CO a.c., mm} \\ \\ (\text{CH}_2)_8 \end{array}$	KOC ₄ H ₉ -t	(12)	49
$\begin{array}{c} (\text{CH}_2)_3\text{CO}_2\text{CH}_3 \\ \\ \text{C}_6\text{H}_5 \\ \\ (\text{CH}_2)_3\text{CO}_2\text{CH}_3 \end{array}$	$\begin{array}{c} (\text{CH}_2)_3\text{C}_6\text{H}_4(\text{CH}_2)_3 \text{ a.c., mm} \\ \quad \quad \\ \text{OC} \quad \quad \text{CO} \\ \quad \quad \\ (\text{CH}_2)_3\text{C}_6\text{H}_4(\text{CH}_2)_3 \end{array}$	KOC ₄ H ₉ -t	(11)	51
$\begin{array}{c} \text{CH}_3\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5 \\ \\ (\text{CH}_2)_8 \\ \\ \text{CH}_3\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5 \end{array}$	$\begin{array}{c} (\text{CH}_2)_{10} \\ \\ \text{OC} \quad \text{CO a.c., mm., oo} \\ \\ (\text{CH}_2)_{10} \end{array}$	KOC ₄ H ₉ -t	(23)	49

Note: References 231 to 583 are on pp. 197-203.

^a This product was isolated after hydrolysis and decarboxylation.

^c Alcohol was removed by azeotropic distillation with the solvent.

^{mm} The reaction was conducted under high-dilution conditions.

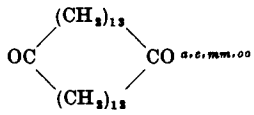
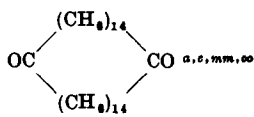
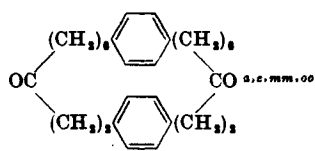
^{mm} The dimeric ketone was also obtained; see below.

^{oo} The monomeric ketone was also obtained; see above.

TABLE II—Continued
CONDENSATIONS LEADING TO CARBOCYCLIC PRODUCTS

E. Condensations Leading to Eight-Membered and Larger Rings—Continued

Starting Ester	Product(s)	Base	Yield (%)	Refs.
$\begin{array}{c} \text{CH}_3\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5 \\ \\ (\text{CH}_2)_7 \\ \\ \text{CH}_3\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5 \end{array}$	$\begin{array}{c} (\text{CH}_2)_{11} \\ \\ \text{OC} \quad \text{CO a.c., mm., oo} \\ \\ (\text{CH}_2)_{11} \end{array}$	KOC ₄ H ₉ -t	(16)	49
$\begin{array}{c} \text{CH}_3\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5 \\ \\ (\text{CH}_2)_8 \\ \\ \text{CH}_3\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5 \end{array}$	$\begin{array}{c} (\text{CH}_2)_{12} \\ \\ \text{OC} \quad \text{CO a.c., mm., oo} \\ \\ (\text{CH}_2)_{12} \end{array}$	KOC ₄ H ₉ -t	(19)	49
$\begin{array}{c} (\text{CH}_2)_4\text{CO}_2\text{CH}_3 \\ \\ \text{C}_6\text{H}_5 \\ \\ (\text{CH}_2)_4\text{CO}_2\text{CH}_3 \end{array}$	$\begin{array}{c} (\text{CH}_2)_4\text{C}_6\text{H}_4(\text{CH}_2)_4 \text{ a.c., mm} \\ \quad \quad \\ \text{OC} \quad \quad \text{CO} \\ \quad \quad \\ (\text{CH}_2)_4\text{C}_6\text{H}_4(\text{CH}_2)_4 \end{array}$	KOC ₄ H ₉ -t	(8.2)	51

$\begin{array}{c} \text{CH}_3\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5 \\ \\ (\text{CH}_2)_2 \\ \\ \text{CH}_3\text{CH}_2\text{CO}_2\text{CH}_3 \end{array}$		KOC_4H_9-t (2)	49
$\begin{array}{c} \text{CH}_3\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5 \\ \\ (\text{CH}_2)_{10} \\ \\ \text{CH}_3\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5 \end{array}$		KOC_4H_9-t (0.9)	49
$\begin{array}{c} (\text{CH}_2)_2\text{CO}_2\text{CH}_3 \\ \\ \text{C}_6\text{H}_5 \\ \\ (\text{CH}_2)_2\text{CO}_2\text{CH}_3 \end{array}$		KOC_4H_9-t (1.2)	51

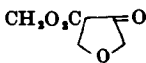
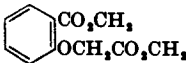
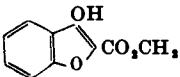
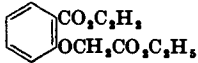
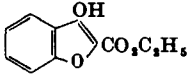
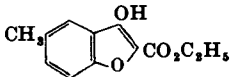
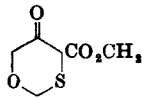

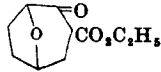
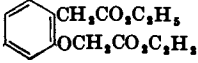
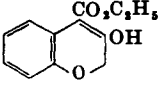
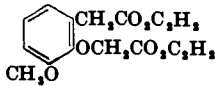
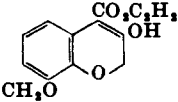


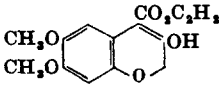
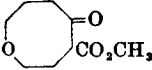
Note: References 231 to 583 are on pp. 197-203.

- * This product was isolated after hydrolysis and decarboxylation.
- * Alcohol was removed by azeotropic distillation with the solvent.
- ^{mm} The reaction was conducted under high-dilution conditions.
- ^{oo} The monomeric ketone was also obtained; see above.


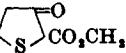
TABLE III
DIECKMANN CONDENSATIONS LEADING TO HETEROCYCLES

122

ORGANIC REACTIONS

A. Heterocycles Containing Oxygen				
Starting Ester	Product(s)	Base	Yield (%)	Refs.
$\text{CH}_3\text{CH}_2\text{CO}_2\text{CH}_3$ $\text{OCH}_2\text{CO}_2\text{CH}_3$		NaOCH_3	(55)	573
		Na	(—)	255
		Na MOC_2H_5^a	(60-70) (—)	288, 255 12
$\text{CH}_3\text{C}_6\text{H}_4\text{CO}_2\text{C}_2\text{H}_5$ $\text{OCH}_2\text{CO}_2\text{C}_2\text{H}_5$		Na	(Quant.)	289
$\text{SCH}_2\text{CO}_2\text{CH}_3$ CH_2 $\text{OCH}_2\text{CO}_2\text{CH}_3$		NaOCH_3	(43)	224
$\text{C}_6\text{H}_5\text{O}_2\text{C}$  $\text{CH}_2\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5$		NaOC_2H_5	(—)	404
		Na	(40)	54, 55
		Na	(56)	558
CH_3O  $\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5$ CH_3O  $\text{OCH}_2\text{CO}_2\text{C}_2\text{H}_5$		Na	(50)	570
$\text{CH}_3\text{CH}_2\text{CH}_2\text{CO}_2\text{CH}_3$ O $\text{CH}_2\text{CH}_2\text{CH}_2\text{CO}_2\text{CH}_3$		$\text{KOC}_2\text{H}_5 \cdot t^b$	(19)	569

B1. Heterocycles Containing Sulfur in a Five-Membered Ring

C_2 $\text{CH}_3\text{CH}_2\text{CO}_2\text{CH}_3$ $\text{SCH}_2\text{CO}_2\text{CH}_3$	A  or B 	NaOCH_3 Na NaNH_2	(A, 94) (B, 74) (B, —) (B, —)	108,° 267 573, 108,° 267, 382 421, 383 421
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Note: References 231 to 583 are on pp. 197-203.

^a Various metal ethoxides were used.

^b This reaction was done under high-dilution conditions.

^c This reference points out that the product depends on the temperature of the reaction mixture. In refluxing toluene, compound A, 4-carbalkoxy-3-ketothiophane, is produced. In refluxing ether (and at lower temperatures in other solvents) the product is the 2-carbalkoxy derivative. The products listed are the ones suggested by the references given. In some cases they are probably incorrect.


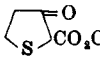
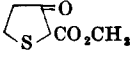
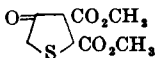

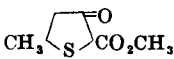
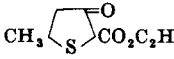
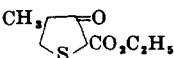
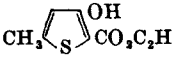
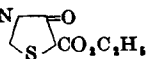
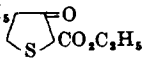
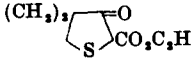
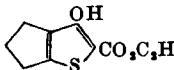
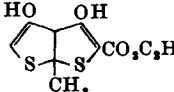
THE DIECKMANN CONDENSATION

123

TABLE III—Continued
DIECKMANN CONDENSATIONS LEADING TO HETEROCYCLES

124

ORGANIC REACTIONS

B1. Heterocycles Containing Sulfur in a Five-Membered Ring—Continued				
Starting Ester	Product(s)	Base	Yield (%)	Refs.
<i>C₂</i> (contd.)				
$\begin{array}{c} \text{CH}_2\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5 \\ \\ \text{SCH}_2\text{CO}_2\text{C}_2\text{H}_5 \end{array}$	A $\text{C}_2\text{H}_5\text{O}_2\text{C}$  or	Na	(B, —)	421
	B  $\text{CO}_2\text{C}_2\text{H}_5$	Na NaNH ₂ NaOC ₂ H ₅ NaOC ₂ H ₅	(A, —) (B, —) (A, 57–64) (A, 72) (B, good)	301 366 258, 286 258 345
$\begin{array}{c} \text{CH}_2\text{CO}_2\text{CH}_3 \\ \\ \text{CHCO}_2\text{CH}_3 \\ \\ \text{SCH}_2\text{CO}_2\text{CH}_3 \end{array}$	 CO_2CH_3	NaOCH ₃	(Good)	345
$\begin{array}{c} \text{CH}_2\text{CO}_2\text{CH}_3 \\ \\ \text{CHCO}_2\text{CH}_3 \\ \\ \text{SCH}_2\text{CO}_2\text{CH}_3 \end{array}$	 CO_2CH_3	NaOCH ₃	(56–63)	80, ⁴ 369
$\begin{array}{c} \text{CH}_2\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5 \\ \\ \text{SCH}(\text{CH}_3)\text{CO}_2\text{C}_2\text{H}_5 \end{array}$	$\text{C}_2\text{H}_5\text{O}_2\text{C}$  CH_3	Na NaNH ₂	(—) (49)	301 451
$\begin{array}{c} \text{CH}(\text{CH}_3)\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5 \\ \\ \text{SCH}_2\text{CO}_2\text{CH}_3 \end{array}$	CH_3  CO_2CH_3	NaOCH ₃	(35)	323
$\begin{array}{c} \text{CH}(\text{CH}_3)\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5 \\ \\ \text{SCH}_2\text{CO}_2\text{C}_2\text{H}_5 \end{array}$	CH_3  $\text{CO}_2\text{C}_2\text{H}_5$	Na	(12)	250, 371
<i>C₃</i>				
$\begin{array}{c} \text{CH}_2\text{CH}(\text{CH}_3)\text{CO}_2\text{C}_2\text{H}_5 \\ \\ \text{SCH}_2\text{CO}_2\text{C}_2\text{H}_5 \end{array}$	CH_3  $\text{CO}_2\text{C}_2\text{H}_5$	Na	(—)	370
$\begin{array}{c} \text{CH}_2\text{C}(\text{OH})\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5 \\ \\ \text{SCH}_2\text{CO}_2\text{C}_2\text{H}_5 \end{array}$	CH_3  $\text{CO}_2\text{C}_2\text{H}_5$	NaOC ₂ H ₅	(24)	250
<i>C₄</i>				
$\begin{array}{c} \text{CH}_2\text{CH}(\text{NHCOCH}_3)\text{CO}_2\text{C}_2\text{H}_5 \\ \\ \text{SCH}_2\text{CO}_2\text{C}_2\text{H}_5 \end{array}$	CH_3COHN  $\text{CO}_2\text{C}_2\text{H}_5$	NaNH ₂	(36)	568
$\begin{array}{c} \text{CH}_2\text{CH}(\text{C}_2\text{H}_5)\text{CO}_2\text{C}_2\text{H}_5 \\ \\ \text{SCH}_2\text{CO}_2\text{C}_2\text{H}_5 \end{array}$	C_2H_5  $\text{CO}_2\text{C}_2\text{H}_5$	Na	(66)	256
$\begin{array}{c} \text{CH}_2\text{C}(\text{CH}_3)_2\text{CO}_2\text{C}_2\text{H}_5 \\ \\ \text{SCH}_2\text{CO}_2\text{C}_2\text{H}_5 \end{array}$	$(\text{CH}_3)_2$  $\text{CO}_2\text{C}_2\text{H}_5$	NaOC ₂ H ₅	(66)	176
<i>C₅</i>				
$\begin{array}{c} \text{Cyclopentyl} \text{CO}_2\text{C}_2\text{H}_5 \\ \\ \text{SCH}_2\text{CO}_2\text{C}_2\text{H}_5 \end{array}$	 $\text{CO}_2\text{C}_2\text{H}_5$	NaOC ₂ H ₅	(—)	580
$\begin{array}{c} \text{SCH}_2\text{CO}_2\text{C}_2\text{H}_5 \\ \\ \text{C}(\text{CH}_3)_2\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5 \\ \\ \text{SCH}_2\text{CO}_2\text{C}_2\text{H}_5 \end{array}$	 $\text{CO}_2\text{C}_2\text{H}_5$	NaOC ₂ H ₅	(47)	250

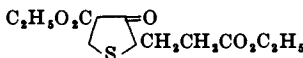
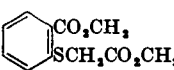
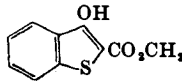
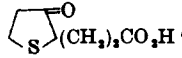
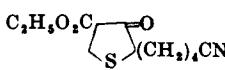
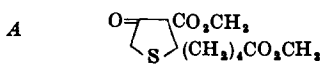
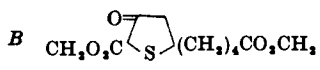
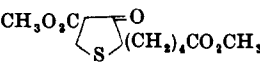
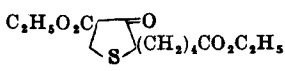
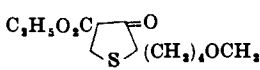
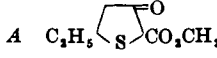
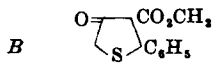
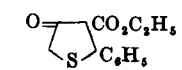
Note: References 231 to 583 are on pp. 197–203.

⁴ The authors of Ref. 80 established the structure of the product.

THE DIECKMANN CONDENSATION

125

TABLE III—Continued
DIECKMANN CONDENSATIONS LEADING TO HETEROCYCLES

B1. Heterocycles Containing Sulfur in a Five-Membered Ring—Continued				
Starting Ester	Product(s)	Base	Yield (%)	Refs.
<i>C₈ (contd.)</i>				
CH ₃ CH ₂ CO ₂ C ₂ H ₅ CHCO ₂ C ₂ H ₅ SCH ₂ CH ₂ CO ₂ C ₂ H ₅		NaOC ₂ H ₅	(67)	260
<i>C₉</i>				
		Na NaOCH ₃	(—) (—)	290, 326 326
CH ₃ CH ₂ CH ₂ CO ₂ CH ₃ CHCO ₂ CH ₃ SCH ₂ CH ₂ CO ₂ CH ₃		NaOC ₂ H ₅	(63)	295
<i>C₁₀</i>				
(CH ₂) ₄ CN CHCO ₂ CH ₃ SCH ₂ CH ₂ CO ₂ CH ₃		NaOC ₂ H ₅	(74)	257
(CH ₂) ₄ CO ₂ CH ₃ CHCH ₂ CO ₂ CH ₃ SCH ₂ CO ₂ CH ₃	<i>A</i>  <i>B</i> 	NaOCH ₃	(<i>A</i> , 7)' (<i>B</i> , 67)'	293
(CH ₂) ₄ CO ₂ CH ₃ CHCO ₂ CH ₃ SCH ₂ CH ₂ CO ₂ CH ₃		NaOCH ₃	(75–80)	295
(CH ₂) ₄ CO ₂ C ₂ H ₅ CHCO ₂ C ₂ H ₅ SCH ₂ CH ₂ CO ₂ C ₂ H ₅		NaOC ₂ H ₅	(82–99)	303, 257, 377
(CH ₂) ₄ OCH ₃ CHCO ₂ C ₂ H ₅ SCH ₂ CH ₂ CO ₂ C ₂ H ₅		NaOC ₂ H ₅	(80)	259
<i>C₁₁</i>				
CH(C ₂ H ₅)CH ₂ CO ₂ CH ₃ ^a SCH ₂ CO ₂ CH ₃	<i>A</i>  <i>B</i> 	NaOCH ₃	(<i>A</i> , 40) ^b (<i>B</i> , —) ^b	323 323
CH(C ₂ H ₅)CH ₂ CO ₂ C ₂ H ₅ SCH ₂ CO ₂ C ₂ H ₅		NaOC ₂ H ₅	(30)	574

Note: References 231 to 583 are on pp. 197–203.

^a This product was obtained after hydrolysis and decarboxylation.

^b The relative yields of *A* and *B* depend on the temperature.

^c The methyl-ethyl ester gave similar results.




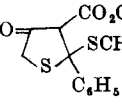

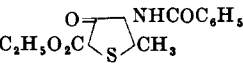


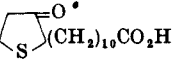
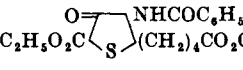
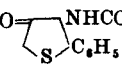
^d Compound *A* was formed in benzene at 40–50°; compound *B* was formed in refluxing toluene.

^e This is the formula given in the reference. It is probably incorrect. See footnotes *c*, *h*.

TABLE III—Continued
DIECKMANN CONDENSATIONS LEADING TO HETEROCYCLES

128

ORGANIC REACTIONS

B1. Heterocycles Containing Sulfur in a Five-Membered Ring—Continued				
Starting Ester	Product(s)	Base	Yield (%)	Refs.
<i>C₁₁ (contd.)</i>				
$(\text{CH}_2)_3\text{CH}_2\text{COCH}_3$ $\text{CHCO}_2\text{C}_2\text{H}_5$ $\text{SCH}_2\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5$	$\text{C}_2\text{H}_5\text{O}_2\text{C}$  $(\text{CH}_2)_3\text{CH}_2\text{COCH}_3$	NaOC_2H_5	(Low)	374
<i>C₁₁</i>				
$\text{CH}_2(\text{NHCOC}_6\text{H}_5)\text{CO}_2\text{CH}_3$ $\text{CH}_2\text{SCH}_2\text{CO}_2\text{CH}_3$	$\text{C}_6\text{H}_5\text{CONH}$  CO_2CH_3	NaOCH_3	(89)	251, 353
$\text{CH}(\text{NHCH}_2\text{C}_6\text{H}_5)\text{CO}_2\text{CH}_3$ $\text{CH}_2\text{SCH}_2\text{CO}_2\text{CH}_3$	$\text{C}_6\text{H}_5\text{CH}_2\text{NH}$  CO_2CH_3	NaOCH_3	(31)	353
<i>C₁₃</i>				
$\text{SCH}_2\text{CO}_2\text{C}_2\text{H}_5$ $\text{C}(\text{C}_6\text{H}_5)\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5$ $\text{SCH}_2\text{CO}_2\text{C}_2\text{H}_5$		NaOC_2H_5	(31)	250
$\text{CH}(\text{NHCOC}_6\text{H}_5)\text{CO}_2\text{CH}_3$ $\text{CH}_2\text{SCH}_2\text{CO}_2\text{CH}_3$	$\text{C}_6\text{H}_5\text{CH}_2\text{CONH}$  CO_2CH_3	NaOCH_3	(79)	353
$\text{CH}_3\text{CHCH}(\text{NHCOC}_6\text{H}_5)\text{CO}_2\text{C}_2\text{H}_5$ $\text{SCH}_2\text{CO}_2\text{C}_2\text{H}_5$		NaOC_2H_5	(31)	577
<i>C₁₆–C₁₈</i>				
$(\text{CH}_2)_3\text{OC}_6\text{H}_5$ $\text{CHCO}_2\text{C}_2\text{H}_5$ $\text{SCH}_2\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5$	$\text{C}_2\text{H}_5\text{O}_2\text{C}$  $(\text{CH}_2)_3\text{OC}_6\text{H}_5$	NaOC_2H_5	(85)	374
$(\text{CH}_2)_4\text{OCH}_2\text{C}_6\text{H}_5$ $\text{CHCO}_2\text{C}_2\text{H}_5$ $\text{SCH}_2\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5$	$\text{C}_2\text{H}_5\text{O}_2\text{C}$  $(\text{CH}_2)_4\text{OCH}_2\text{C}_6\text{H}_5$	NaOC_2H_5	(Good)	374
$(\text{CH}_2)_{10}\text{CO}_2\text{CH}_3$ CHCO_2CH_3 $\text{SCH}_2\text{CH}_2\text{CO}_2\text{CH}_3$		NaOC_2H_5	(68)	425
$(\text{CH}_2)_4\text{CO}_2\text{C}_2\text{H}_5$ $\text{CH}(\text{NHCOC}_6\text{H}_5)\text{CO}_2\text{C}_2\text{H}_5$ $\text{SCH}_2\text{CO}_2\text{C}_6\text{H}_5$	$\text{C}_2\text{H}_5\text{O}_2\text{C}$ 	NaOC_2H_5	(17)	578
$\text{CH}(\text{NHCOC}_6\text{H}_5)\text{CO}_2\text{CH}_3$ $\text{CH}(\text{C}_6\text{H}_5)\text{SCH}_2\text{CO}_2\text{CH}_3$		NaOCH_3	(50)	372

Note: References 231 to 583 are on pp. 197–203.

* This product was obtained after hydrolysis and decarboxylation.

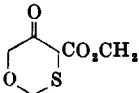
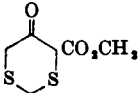
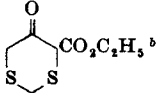
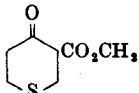

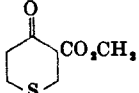
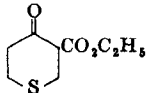
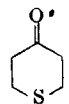
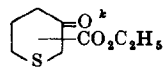
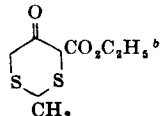
THE DIECKMANN CONDENSATION

129

TABLE III—Continued
DIECKMANN CONDENSATIONS LEADING TO HETEROCYCLES

130

ORGANIC REACTIONS

B2. Heterocycles Containing Sulfur in a Six-Membered Ring				
Starting Ester	Product(s)	Base	Yield (%)	Refs.
$\begin{array}{c} \text{C}_6\text{H}_5 \\ \\ \text{SCH}_2\text{CO}_2\text{CH}_3 \\ \\ \text{CH}_2\text{OCH}_2\text{CO}_2\text{CH}_3 \end{array}$		NaOCH ₃	(22-43) ⁱ	224
$\begin{array}{c} \text{SCH}_2\text{CO}_2\text{CH}_3 \\ \\ \text{CH}_2 \\ \\ \text{SCH}_2\text{CO}_2\text{CH}_3 \end{array}$		NaOCH ₃	(—)	322
$\begin{array}{c} \text{SCH}_2\text{CO}_2\text{C}_2\text{H}_5 \\ \\ \text{CH}_2 \\ \\ \text{SCH}_2\text{CO}_2\text{C}_2\text{H}_5 \end{array}$		NaH	(82)	58
$\begin{array}{c} \text{C}_6\text{H}_5 \\ \\ \text{CH}_2\text{CH}_2\text{CO}_2\text{CH}_3 \\ \\ \text{S} \\ \\ \text{CH}_2\text{CH}_2\text{CO}_2\text{CH}_3 \end{array}$		NaOCH ₃	(65)	56, 249
		NaOCH ₃	(50-55)	298
$\begin{array}{c} \text{CH}_2\text{CH}_2\text{CO}_2\text{CH}_3 \\ \\ \text{S} \\ \\ \text{CH}_2\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5 \end{array}$		NaOCH ₃	(Good)	345
$\begin{array}{c} \text{CH}_2\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5 \\ \\ \text{S} \\ \\ \text{CH}_2\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5 \end{array}$		NaNH ₂ NaOC ₂ H ₅	(40) (43)	579 300
		NaOC ₂ H ₅	(21)	582
$\begin{array}{c} \text{CH}_2\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5 \\ \\ \text{CH}_2\text{SCH}_2\text{CO}_2\text{C}_2\text{H}_5 \end{array}$		NaOC ₂ H ₅	(75)	329
$\begin{array}{c} \text{SCH}_2\text{CO}_2\text{C}_2\text{H}_5 \\ \\ \text{CHCH}_3 \\ \\ \text{SCH}_2\text{CO}_2\text{C}_2\text{H}_5 \end{array}$		NaH	(77-80)	58

Note: References 231 to 583 are on pp. 197-203.

^b This reaction was done under high-dilution conditions.

^c This product was obtained after hydrolysis and decarboxylation.

ⁱ A yield of 43% was obtained in ether at 0°. The yield was 22% in toluene at 80°.

^{*} The product was either the 2- or the 4-carbethoxy compound.

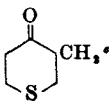
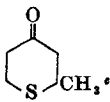
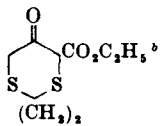
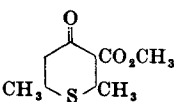
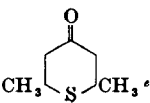
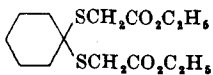
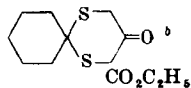
131

THE DIECKMANN CONDENSATION

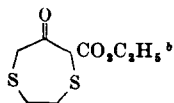
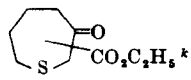
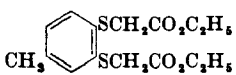
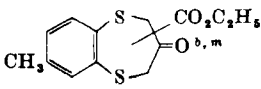
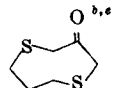
TABLE III—Continued
DIECKMANN CONDENSATIONS LEADING TO HETEROCYCLES

132

ORGANIC REACTIONS

B2. Heterocycles Containing Sulfur in a Six-Membered Ring—Continued				
Starting Ester	Product(s)	Base	Yield (%)	Refs.
C ₇ CH ₂ CH(CH ₃)CO ₂ C ₂ H ₅ SCH ₂ CH ₂ CO ₂ C ₂ H ₅		NaOCH ₃	(26)	298
CH(CH ₃)CH ₂ CO ₂ CH ₃ SCH ₂ CH ₂ CO ₂ CH ₃		NaOCH ₃	(25)	298
SCH ₂ CO ₂ C ₂ H ₅ C(CH ₃) ₂ SCH ₂ CO ₂ C ₂ H ₅		NaH	(80)	58
C ₈ –C ₁₀ CH(CH ₃)CH ₂ CO ₂ CH ₃ S CH(CH ₃)CH ₂ CO ₂ CH ₃		NaOCH ₃	(33)	298
		NaOCH ₃	(24)	298
		NaH	(80–83)	58

B3. Heterocycles Containing Sulfur in Seven-Membered and Larger Rings

CH ₂ SCH ₂ CO ₂ C ₂ H ₅ CH ₂ SCH ₂ CO ₂ C ₂ H ₅		NaH KOC ₄ H ₉ -t	(10–20) ⁱ (45)	58 58
CH ₂ CH ₂ CH ₂ CO ₂ C ₂ H ₅ CH ₂ SCH ₂ CO ₂ C ₂ H ₅		NaOC ₂ H ₅	(23)	329
		KOC ₄ H ₉ -t NaH	(35–40) (10–15)	58 58
CH ₂ SCH ₂ CO ₂ C ₂ H ₅ CH ₂ CH ₂ SCH ₂ CO ₂ C ₂ H ₅		KOC ₄ H ₉ -t	(2–3)	58

Note: References 231 to 583 are on pp. 197–203.

^b This reaction was done under high-dilution conditions.

^c This product was obtained after hydrolysis and decarboxylation.

^d The product was either the 2- or the 4-carbomethoxy compound.

ⁱ The reaction was run in benzene and in tetrahydrofuran. The better yield was obtained in benzene.

^m The position of the carbomethoxyl group was not established.


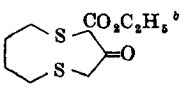
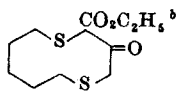
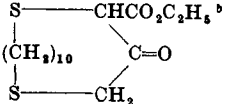
133

THE DIECKMANN CONDENSATION

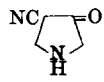
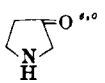
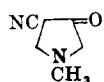
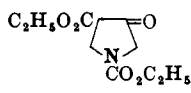
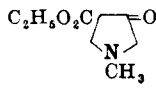
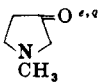
TABLE III—Continued
DIECKMANN CONDENSATIONS LEADING TO HETEROCYCLES

134

ORGANIC REACTIONS

B3. Heterocycles Containing Sulfur in Seven-Membered and Larger Rings—Continued				
Starting Ester	Product(s)	Base	Yield (%)	Refs.
C ₈ –C ₁₀ (contd.) CH ₂ CH ₂ CH ₂ CO ₂ C ₂ H ₅ S CH ₂ CH ₂ CH ₂ CO ₂ C ₂ H ₅	 ^{b, e, n}	KOC ₄ H ₉ -t	(20–45)	331, 569
SCH ₂ CO ₂ C ₂ H ₅ (CH ₂) ₄ SCH ₂ CO ₂ C ₂ H ₅	 ^b	KOC ₄ H ₉ -t	(0)	58
SCH ₂ CO ₂ C ₂ H ₅ (CH ₂) ₄ SCH ₂ CO ₂ C ₂ H ₅	 ^b	KOC ₄ H ₉ -t	(5–8)	58
SCH ₂ CO ₂ C ₂ H ₅ (CH ₂) ₁₀ SCH ₂ CO ₂ C ₂ H ₅	 ^b	KOC ₄ H ₉ -t	(15–20)	58

C1. Heterocycles Containing Nitrogen in a Five-Membered Ring

C ₄ CH ₂ CH ₂ CN NHCH ₂ CO ₂ C ₂ H ₅		NaOC ₂ H ₅	(15)	559
CH ₂ CH ₂ CO ₂ C ₂ H ₅ NHCH ₂ CO ₂ C ₂ H ₅		Na	(—)	319
C ₄ CH ₂ CH ₂ CN N(CH ₃)CH ₂ CO ₂ C ₂ H ₅		NaOC ₂ H ₅	(—)	411
CH ₂ CH ₂ CO ₂ C ₂ H ₅ N(CO ₂ C ₂ H ₅)CH ₂ CO ₂ C ₂ H ₅		Na	(65)	88, 338
CH ₂ CH ₂ CO ₂ C ₂ H ₅ N(CH ₃)CH ₂ CO ₂ C ₂ H ₅		NaOC ₂ H ₅	(36–70) ^r	133
		NaOC ₂ H ₅	(64)	528

Note: References 231 to 583 are on pp. 197–203.

^b This reaction was done under high-dilution conditions.

^c This product was obtained after hydrolysis and decarboxylation.

ⁿ The addition of the ester required 110 hours. Addition during 25 hours led to a 2% yield of monomer and a 3% yield of dimer.

^e No derivative characteristic of β -pyrrolidone could be obtained.

^r The yield was lower with no solvent; higher in benzene.

^q Alcohol was removed by azeotropic distillation with the solvent.

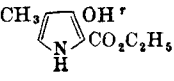
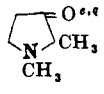
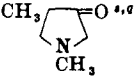
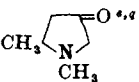
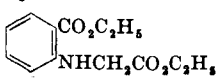
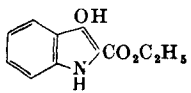
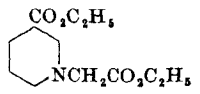
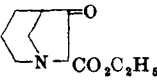
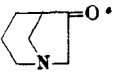
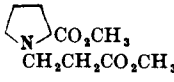

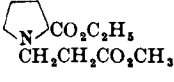

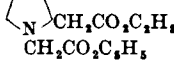
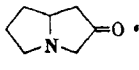
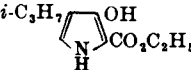
135

THE DIECKMANN CONDENSATION

TABLE III—Continued
DIECKMANN CONDENSATIONS LEADING TO HETEROCYCLES

136

ORGANIC REACTIONS

C1. Heterocycles Containing Nitrogen in a Five-Membered Ring—Continued				
Starting Ester	Product(s)	Base	Yield (%)	Refs.
C ₅ (contd.)				
CH ₂ CH(CH ₃)CO ₂ C ₂ H ₅ NHCH ₂ CO ₂ C ₂ H ₅		K	(23)	305
C ₇				
CH ₂ CH ₂ CO ₂ C ₂ H ₅ NCH ₃ CH(CH ₃)CO ₂ C ₂ H ₅		NaOC ₂ H ₅	(60)	528
CH ₂ CH(CH ₃)CO ₂ C ₂ H ₅ NCH ₃ CH ₂ CO ₂ C ₂ H ₅		NaOC ₂ H ₅	(63)	528
CH(CH ₃)CH ₂ CO ₂ C ₂ H ₅ NCH ₃ CH ₂ CO ₂ C ₂ H ₅		NaOC ₂ H ₅	(70)	528
C ₈				
		NaOC ₂ H ₅	(64–67)	548
C ₈ H ₁₃				
		NaOC ₂ H ₅	(0)	142
		KOC ₂ H ₅ K	(70) (31–36) *	143 145
		NaOC ₂ H ₅	(55)	563
		NaOC ₂ H ₅	(51–65)	563, 555, 575
		K	(68)	305
NHCH ₂ CO ₂ C ₂ H ₅ CH=C(C ₂ H ₅ , i-)CO ₂ C ₂ H ₅		NaOH	(24)	436

Note: References 231 to 583 are on pp. 197–203.

* This product was obtained after hydrolysis and decarboxylation.

* Alcohol was removed by azeotropic distillation with the solvent.

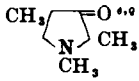
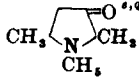
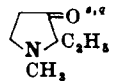
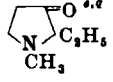
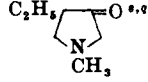

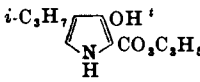

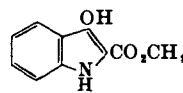

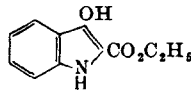
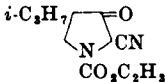
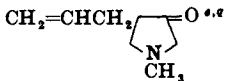
* The pyrrolidone was apparently readily oxidized by air during isolation. The formula shown in the reference and the name applied to the reaction product are inconsistent with the starting material and with the analytical results. The formula shown here is consistent with the experimental data.

* The product was isolated as the hydrochloride.

THE DIECKMANN CONDENSATION

137

TABLE III—Continued
DIECKMANN CONDENSATIONS LEADING TO HETEROCYCLES

C1. Heterocycles Containing Nitrogen in a Five-Membered Ring—Continued				
Starting Ester	Product(s)	Base	Yield (%)	Refs.
C_2H_5 $CH_2CH(CH_3)CO_2C_2H_5$ $ $ NCH_3 $ $ $CH(CH_3)CO_2C_2H_5$ $ $ $CH(CH_3)CH_2CO_2C_2H_5$ $ $ NCH_3 $ $ $CH(CH_3)CO_2C_2H_5$		$NaOC_2H_5$	(12)	528
$CH_2CH_2CO_2CH_3$ $ $ NCH_3 $ $ $CH(C_2H_5)CO_2CH_3$		$NaOC_2H_5$	(54)	528
$CH_2CH_2CO_2CH_3$ $ $ NCH_3 $ $ $CH(C_2H_5)CO_2CH_3$		$NaOC_2H_5$ or K	(82)	514
$CH_2CH_2CO_2C_2H_5$ $ $ NCH_3 $ $ $CH(C_2H_5)CO_2C_2H_5$		$NaOC_2H_5$	(82)	514, 528
$CH_2CH(C_2H_5)CO_2C_2H_5$ $ $ NCH_3 $ $ $CH_2CO_2C_2H_5$		$NaOC_2H_5$	(53)	528
$CH_2CH_2CO_2C_2H_5$ $ $ NC_2H_5 $ $ $CH(CH_3)CO_2C_2H_5$		$NaOC_2H_5$	(38)	528
$CH_2CH(C_2H_5-i)CO_2C_2H_5$ $ $ $NHCH_2CO_2C_2H_5$		$NaOH$	(19)	436
C_6H_5  CO_2CH_3 $ $ $NHCH_2CO_2CH_3$		Na	(50)	350
 $CO_2C_2H_5$ $ $ $NHCH_2CO_2C_2H_5$		Na	(50, 100)	291, 350
CH_2CN $ $ $NCO_2C_2H_5$ $ $ $CH_2CH(C_2H_5-i)CO_2C_2H_5$		Na	(60)	215
C_2H_5 $CH_2CH(CH_2CH=CH_2)CO_2C_2H_5$ $ $ NCH_3 $ $ $CH_2CO_2C_2H_5$		$NaOC_2H_5$	(35)	528

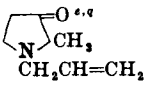
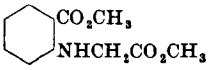
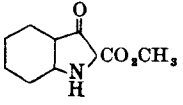
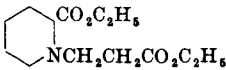
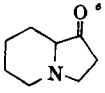
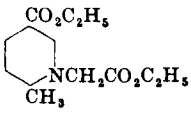
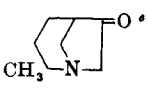
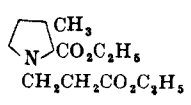
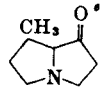
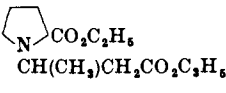
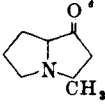
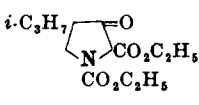


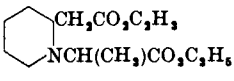
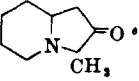
Note: References 231 to 583 are on pp. 197–203.

* This product was obtained after hydrolysis and decarboxylation.

* Alcohol was removed by azeotropic distillation with the solvent.

* Oxidation by air during the isolation of the product gave the pyrrole.

TABLE III—Continued
DIECKMANN CONDENSATIONS LEADING TO HETEROCYCLES

C1. Heterocycles Containing Nitrogen in a Five-Membered Ring—Continued				
Starting Ester	Product(s)	Base	Yield (%)	Refs.
<i>C₉H₁₅ (contd.)</i>				
$\text{CH}_2\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5$ $\text{NCH}_2\text{CH}=\text{CH}_2$ $\text{CH}(\text{CH}_3)\text{CO}_2\text{C}_2\text{H}_5$		NaOC_2H_5	(70)	528
		NaOCH_3	(1-2)	552
		NaOC_2H_5 Na	(62) (66)	57 501
		KOC_2H_5	(72)	565
		K	(59)	513
		NaH	(50)	514
$\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5$ $\text{NCO}_2\text{C}_2\text{H}_5$ $\text{CH}_2\text{CH}(\text{C}_3\text{H}_7-i)\text{CO}_2\text{C}_2\text{H}_5$		Na	(60)	215
<i>C₉H₁₇</i>				
$\text{CH}_2\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5$ NC_3H_7-i $\text{CH}(\text{CH}_3)\text{CO}_2\text{C}_2\text{H}_5$		NaOC_2H_5	(60)	528
$\text{CH}_2\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5$ NC_4H_9-n $\text{CH}_2\text{CO}_2\text{C}_3\text{H}_7$		NaOC_2H_5	(73)	514
<i>C₁₀-C₁₂</i>				
		K	(68-71)	328, 502

Note: References 231 to 583 are on pp. 197-203.

* This product was obtained after hydrolysis and decarboxylation.

* Alcohol was removed by azeotropic distillation with the solvent.

TABLE III—Continued
DIECKMANN CONDENSATIONS LEADING TO HETEROCYCLES

142

ORGANIC REACTIONS

C1. Heterocycles Containing Nitrogen in a Five-Membered Ring—Continued					
Starting Ester	Product(s)	Base	Yield (%)	Refs.	
C ₁₀ –C ₁₂ (contd.)					
		NaOC ₂ H ₅	(—)	548	
		NaH	(Good)	341	
		Na	(—)	332	
		NaOC ₂ H ₅	(56)	528	
C ₁₃ –C ₁₆					
		NaOC ₂ H ₅	(48)	62	
		Na	(25)	332	
		NaOC ₂ H ₅	(66)	528	
		NaOC ₂ H ₅	(—)	548	
C2. Heterocycles Containing Nitrogen in a Six-Membered Ring					
C ₅ –C ₇					
		Na	(11)	233, 315, 376	

Note: References 231 to 583 are on pp. 197–203.

* This product was obtained after hydrolysis and decarboxylation.

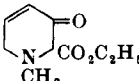
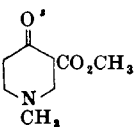
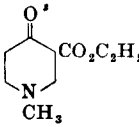
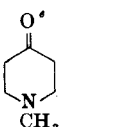
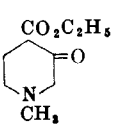
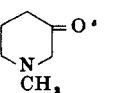
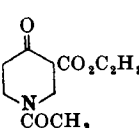
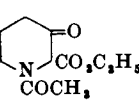
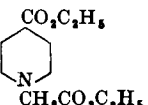
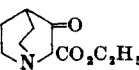
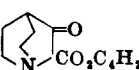
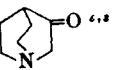
* Alcohol was removed by azeotropic distillation with the solvent.

* The product was isolated as the hydrochloride.

THE DIECKMANN CONDENSATION

143

TABLE III—Continued
DIECKMANN CONDENSATIONS LEADING TO HETEROCYCLES

C2. Heterocycles Containing Nitrogen in a Six-Membered Ring—Continued				
Starting Ester	Product(s)	Base	Yield (%)	Refs.
<i>C₆–C₇ (contd.)</i>				
CH ₂ CH=CHCO ₂ C ₂ H ₅ NCH ₃ CH ₂ CO ₂ C ₂ H ₅		KOC ₄ H ₉ - <i>t</i>	(52)	549
CH ₂ CH ₂ CO ₂ CH ₃ NCH ₃ CH ₂ CH ₂ CO ₂ CH ₃		NaOCH ₃	(70)	566, 411
CH ₂ CH ₂ CO ₂ C ₂ H ₅ NCH ₃ CH ₂ CH ₂ CO ₂ C ₂ H ₅		Na NaH NaOC ₂ H ₅	(57–78) (91) (62–71)	316, 318 334 133
		Na	(40–60)	581
CH ₂ CH ₂ CH ₂ CO ₂ C ₂ H ₅ NCH ₃ CH ₂ CO ₂ C ₂ H ₅		NaOC ₂ H ₅	(74, 85)	133, 519
<i>C₈</i>				
CH ₂ CH ₂ CO ₂ C ₂ H ₅ NCOCH ₃ CH ₂ CH ₂ CO ₂ C ₂ H ₅		NaOC ₂ H ₅	(—)	325
CH ₂ CH ₂ CH ₂ CO ₂ C ₂ H ₅ NCOCH ₃ CH ₂ CO ₂ C ₂ H ₅		Na	(72)	233, 337
CH ₂ CH ₂ CH ₂ CO ₂ C ₂ H ₅ NCOCH ₃ CH ₂ CO ₂ C ₂ H ₅		KOC ₄ H ₉ - <i>t</i>	(45)	549
		KOC ₂ H ₅	(75)	567
		KOC ₃ H ₇ - <i>n</i> ^u	(44)	217
		K	(37–44)	145, 304

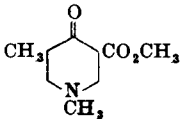
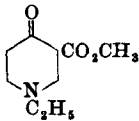
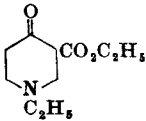
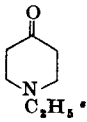
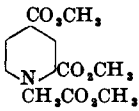
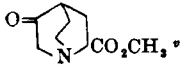
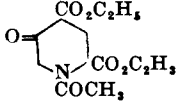
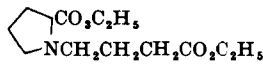
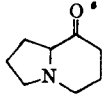
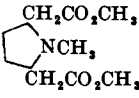
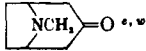
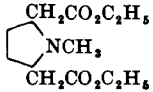
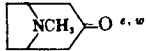
Note: References 231 to 583 are on pp. 197–203.

^a This product was obtained after hydrolysis and decarboxylation.

^b The product was isolated as the hydrochloride.

^u The alkoxide was prepared by distilling water from a mixture of potassium hydroxide, *n*-butanol, and toluene.

TABLE III—Continued
DIECKMANN CONDENSATIONS LEADING TO HETEROCYCLES

C2. Heterocycles Containing Nitrogen in a Six-Membered Ring—Continued				
Starting Ester	Product(s)	Base	Yield (%)	Refs.
<i>C₈ (contd.)</i>				
$\begin{array}{c} \text{CH}_2\text{CH}(\text{CH}_3)\text{CO}_2\text{CH}_3 \\ \\ \text{NCH}_3 \\ \\ \text{CH}_2\text{CH}_2\text{CO}_2\text{CH}_3 \end{array}$		NaOCH ₃	(67)	543
$\begin{array}{c} \text{CH}_2\text{CH}_2\text{CO}_2\text{CH}_3 \\ \\ \text{N}(\text{C}_2\text{H}_5)\text{CH}_2\text{CH}_2\text{CO}_2\text{CH}_3 \end{array}$		NaOCH ₃	(92)	566
$\begin{array}{c} \text{CH}_2\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5 \\ \\ \text{N}(\text{C}_2\text{H}_5)\text{CH}_2\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5 \end{array}$		Na	(50–78) ^a	316, 321
		Na	(82–87)	524, ^a 581
<i>C₉</i>				
		KOCH ₃	(61)	562
$\begin{array}{c} \text{CH}_2\text{CO}_2\text{C}_2\text{H}_5 \\ \\ \text{NCOCH}_3 \\ \\ \text{CH}(\text{CO}_2\text{C}_2\text{H}_5)\text{CH}_2\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5 \end{array}$		Na	(35)	479
		NaOC ₂ H ₅	(41)	57
		Na	(7)	294, 561
		Na KOC ₂ H ₅ , ^t NaNH ₂ NaOC ₂ H ₅	(10, 25) (27) (Poor) (Poor)	561, 422 545 294 294

Note: References 231 to 583 are on pp. 197–203.

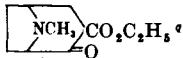
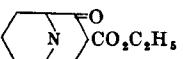
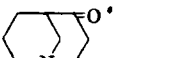
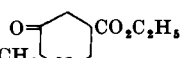

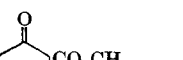
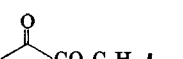


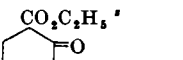
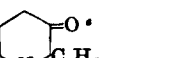
^a This product was obtained after hydrolysis and decarboxylation.

^t The product was isolated as the hydrochloride.

^b This product was obtained after hydrolysis, decarboxylation, and reesterification.

^w The product was isolated as the picrate.

TABLE III—Continued
DIECKMANN CONDENSATIONS LEADING TO HETEROCYCLES

C2. Heterocycles Containing Nitrogen in a Six-Membered Ring—Continued				
Starting Ester	Product(s)	Base	Yield (%)	Refs.
<i>C₂ (contd.)</i>				
$\begin{array}{c} \text{CH}_2\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5 \\ \\ \text{NCH}_3 \\ \\ \text{CO}_2\text{C}_2\text{H}_5 \end{array}$		NaOC ₂ H ₅	(84)	404
$\begin{array}{c} \text{CO}_2\text{C}_2\text{H}_5 \\ \\ \text{N} \\ \\ \text{CH}_2\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5 \end{array}$		Na	(6-7)	252
		KOC ₂ H ₅ NaOC ₂ H ₅ K	(48) (0) (23)*	144 142 145
$\begin{array}{c} \text{CH}_2\text{CH}(\text{CO}_2\text{C}_2\text{H}_5)\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5 \\ \\ \text{NCH}_3 \\ \\ \text{CH}(\text{CH}_3)\text{CO}_2\text{C}_2\text{H}_5 \end{array}$		NaOC ₂ H ₅	(69)	551
$\begin{array}{c} \text{CH}_2\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5 \\ \\ \text{NCH}_2\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5 \\ \\ \text{CH}_2\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5 \end{array}$		Na NaOC ₂ H ₅	(Poor) (46)	319 319
$\begin{array}{c} \text{CH}_2\text{CH}_2\text{CO}_2\text{CH}_3 \\ \\ \text{NC}_3\text{H}_7\text{-}n \\ \\ \text{CH}_2\text{CH}_2\text{CO}_2\text{CH}_3 \end{array}$		CH ₃ ONa	(78)	566
$\begin{array}{c} \text{CH}_2\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5 \\ \\ \text{NC}_3\text{H}_7\text{-}n \\ \\ \text{CH}_2\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5 \end{array}$		Na	(50-78)	316, 321
$\begin{array}{c} \text{CH}_2\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5 \\ \\ \text{NC}_3\text{H}_7\text{-}i \\ \\ \text{CH}_2\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5 \end{array}$		Na	(50-60)	321
		NaH	(—)	335
$\begin{array}{c} \text{CH}_2\text{CH}_2\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5 \\ \\ \text{NCH}_3 \\ \\ \text{CH}(\text{C}_2\text{H}_5)\text{CO}_2\text{C}_2\text{H}_5 \end{array}$		NaOC ₂ H ₅	(66)	324
		K	(51)	324

Note: References 231 to 583 are on pp. 197-203.

* This product was obtained after hydrolysis and decarboxylation.

° Alcohol was removed by azeotropic distillation with the solvent.

* The product was isolated as the hydrochloride.

* This product was obtained after hydrolysis, decarboxylation, and reesterification.

TABLE III—Continued
DIECKMANN CONDENSATIONS LEADING TO HETEROCYCLES

150

ORGANIC REACTIONS

C2. Heterocycles Containing Nitrogen in a Six-Membered Ring—Continued				
Starting Ester	Product(s)	Base	Yield (%)	Refs.
<i>C₃ (contd.)</i>				
$\text{CH}_2\text{CH}_2\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5$ NCH_3 $\text{C}(\text{CH}_3)_2\text{CO}_2\text{C}_2\text{H}_5$		NaOC_2H_5	(50)	325
<i>C₁₀</i>				
		Na	(48)	333
		K	(60)	499
		Na	(50)	308
		NaOC_2H_5	(85)	57
		K	(36)	499
		K	(21, 40)	328, 502
		K	(28)	145
		Na	(18)	545
$\text{CH}_2\text{CH}_2\text{CO}_2\text{CH}_3$ $\text{NC}_6\text{H}_5 \cdot n$ $\text{CH}_2\text{CH}_2\text{CO}_2\text{CH}_3$		NaOCH_3	(80)	566
$\text{CH}_2\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5$ $\text{NC}_6\text{H}_5 \cdot n$ $\text{CH}_2\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5$		Na	(50–78)	316, 321
		NaH	(—)	335

Note: References 231 to 583 are on pp. 197–203.

* This product was obtained after hydrolysis and decarboxylation.

* The product was isolated as the hydrochloride.

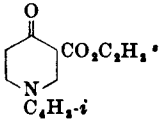
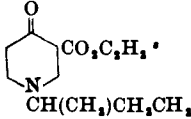
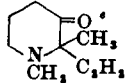
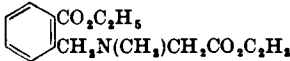
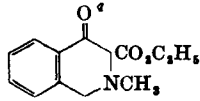
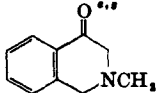
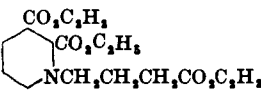
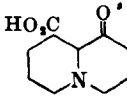
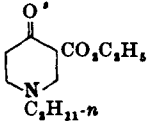
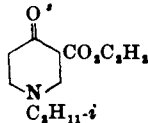
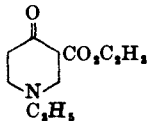
THE DIECKMANN CONDENSATION

151

TABLE III—Continued
DIECKMANN CONDENSATIONS LEADING TO HETEROCYCLES

152

ORGANIC REACTIONS

C2. Heterocycles Containing Nitrogen in a Six-Membered Ring—Continued				
Starting Ester	Product(s)	Base	Yield (%)	Refs.
C ₁₀ (contd.)				
$\begin{array}{c} \text{CH}_3\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5 \\ \\ \text{NC}_4\text{H}_9-i \\ \\ \text{CH}_3\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5 \end{array}$		Na	(50–60)	321
$\begin{array}{c} \text{CH}_3\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5 \\ \\ \text{NCH}(\text{CH}_3)\text{CH}_2\text{CH}_3 \\ \\ \text{CH}_3\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5 \end{array}$		Na	(50–60)	321
$\begin{array}{c} \text{CH}_3\text{CH}_2\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5 \\ \\ \text{NCH}_3 \\ \\ \text{C}(\text{CH}_3)\text{CH}_2\text{CH}_3 \\ \\ \text{CO}_2\text{C}_2\text{H}_5 \end{array}$		NaOC ₂ H ₅	(46)* (55)	325 542
C ₁₁				
		NaOC ₂ H ₅	(—)	481
		Na	(31)	481
		Na	(—)	311
$\begin{array}{c} \text{CH}_3\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5 \\ \\ \text{NC}_4\text{H}_{11-n} \\ \\ \text{CH}_3\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5 \end{array}$		Na	(50–78)	316, 321
$\begin{array}{c} \text{CH}_3\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5 \\ \\ \text{NC}_4\text{H}_{11-i} \\ \\ \text{CH}_3\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5 \end{array}$		Na	(50–60)	321
C ₁₂				
$\begin{array}{c} \text{CH}_3\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5 \\ \\ \text{NC}_2\text{H}_5 \\ \\ \text{CH}_3\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5 \end{array}$		Na	(70)	336

Note: References 231 to 583 are on pp. 197–203.

- * This product was obtained after hydrolysis and decarboxylation.
- * Alcohol was removed by azeotropic distillation with the solvent.
- * The product was isolated as the hydrochloride.

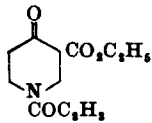
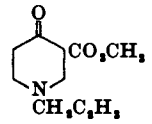
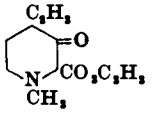
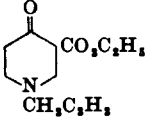
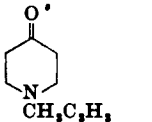
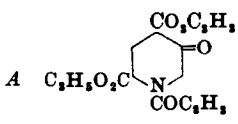
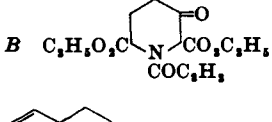
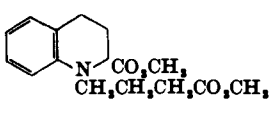
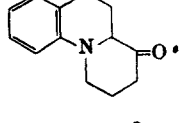
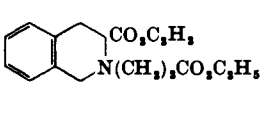
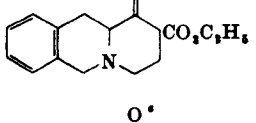
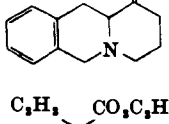
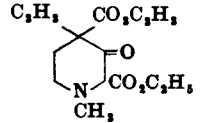
THE DIECKMANN CONDENSATION

153

TABLE III—Continued
DIECKMANN CONDENSATIONS LEADING TO HETEROCYCLES

154

ORGANIC REACTIONS

C2. Heterocycles Containing Nitrogen in a Six-Membered Ring—Continued				
Starting Ester	Product(s)	Base	Yield (%)	Refs.
C ₁₃ CH ₃ CH ₂ CO ₂ C ₂ H ₅ NCOC ₂ H ₅ CH ₃ CH ₂ CO ₂ C ₂ H ₅		Na NaH	(66–68) (92)	337, 376 516
CH ₃ CH ₂ CO ₂ CH ₃ NCH ₂ C ₂ H ₅ CH ₃ CH ₂ CO ₂ CH ₃		NaOCH ₃	(—)	566
CH ₃ CO ₂ C ₂ H ₅ NCH ₃ CH ₃ CH ₂ CH(C ₂ H ₅)CO ₂ C ₂ H ₅		NaOC ₂ H ₅ or NaH	(Good)	518
CH ₃ CH ₂ CO ₂ C ₂ H ₅ NCH ₂ C ₂ H ₅ CH ₃ CH ₂ CO ₂ C ₂ H ₅		Na NaOC ₂ H ₅	(50) (83)	336 380*
		NaH	(59)	512
C ₁₄ CH(CO ₂ C ₂ H ₅)CH ₂ CH ₂ CO ₂ C ₂ H ₅ NCOC ₂ H ₅ CH ₂ CO ₂ C ₂ H ₅	A  B 	NaOC ₂ H ₅ NaOC ₂ H ₅	(A, 50–78) (A + B, 75)	546, 479 560
		K	(30)	478
		NaH	(74)	302
		NaOC ₂ H ₅ K NaH	(—) (23) (53)	62 296 302
C ₂ H ₅ C(CO ₂ C ₂ H ₅) ₂ CH ₃ CH ₂ N(CH ₃)CH ₂ CO ₂ C ₂ H ₅		NaOC ₂ H ₅	(47)	518

Note: References 231 to 583 are on pp. 197–203.

- * This product was obtained after hydrolysis and decarboxylation.
- * The product was isolated as the hydrochloride.

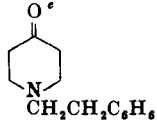
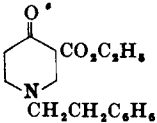
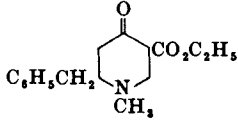
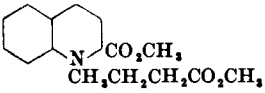
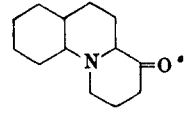
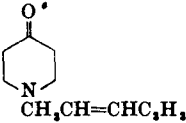
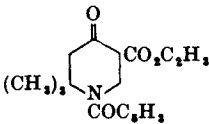
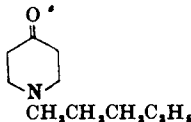
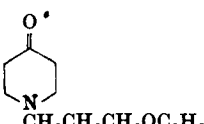
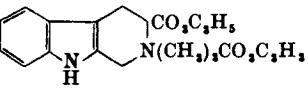
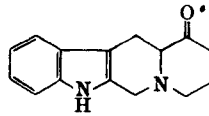
THE DIECKMANN CONDENSATION

155

TABLE III—Continued
DIECKMANN CONDENSATIONS LEADING TO HETEROCYCLES

166

ORGANIC REACTIONS

C2. Heterocycles Containing Nitrogen in a Six-Membered Ring—Continued				
Starting Ester	Product(s)	Base	Yield (%)	Refs.
<i>C₁₁ (contd.)</i>				
$\begin{array}{c} \text{CH}_2\text{CH}_2\text{CO}_2\text{CH}_3 \\ \\ \text{NCH}_2\text{CH}_2\text{C}_6\text{H}_5 \\ \\ \text{CH}_2\text{CH}_2\text{CO}_2\text{CH}_3 \end{array}$		NaH	(70)	512
$\begin{array}{c} \text{CH}_2\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5 \\ \\ \text{NCH}_2\text{CH}_2\text{C}_6\text{H}_5 \\ \\ \text{CH}_2\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5 \end{array}$		Na	(40–50)	316, 336
$\begin{array}{c} \text{CH}(\text{CH}_2\text{C}_6\text{H}_5)\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5 \\ \\ \text{NCH}_3 \\ \\ \text{CH}_2\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5 \end{array}$		NaH	(91)	516
		K	(64)	478
<i>C₁₅</i>				
$\begin{array}{c} \text{CH}_2\text{CH}_2\text{CO}_2\text{CH}_3 \\ \\ \text{NCH}_2\text{CH}=\text{CHC}_6\text{H}_5 \\ \\ \text{CH}_2\text{CH}_2\text{CO}_2\text{CH}_3 \end{array}$		NaH	(70)	512
$\begin{array}{c} \text{CH}_2\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5 \\ \\ \text{NCOC}_6\text{H}_5 \\ \\ \text{C}(\text{CH}_3)_2\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5 \end{array}$		Na	(40)	550
$\begin{array}{c} \text{CH}_2\text{CH}_2\text{CO}_2\text{CH}_3 \\ \\ \text{NCH}_2\text{CH}_2\text{CH}_2\text{C}_6\text{H}_5 \\ \\ \text{CH}_2\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5 \end{array}$		NaH	(43)	512
$\begin{array}{c} \text{CH}_2\text{CH}_2\text{CO}_2\text{CH}_3 \\ \\ \text{NCH}_2\text{CH}_2\text{CH}_2\text{OC}_6\text{H}_5 \\ \\ \text{CH}_2\text{CH}_2\text{CO}_2\text{CH}_3 \end{array}$		NaH	(75)	512
<i>C₁₆</i>				
		K	(47)	489

Note: References 231 to 583 are on pp. 197–203.

- * This product was obtained after hydrolysis and decarboxylation.
- * The product was isolated as the hydrochloride.

167

THE DIECKMANN CONDENSATION

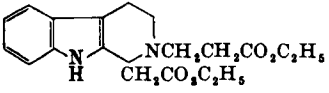
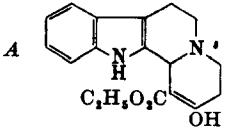
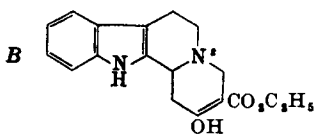
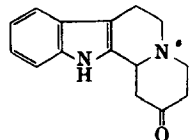
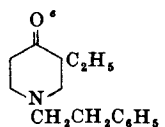
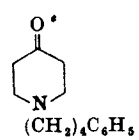
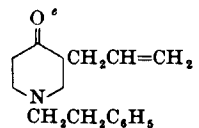
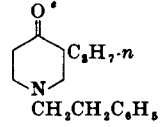
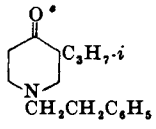
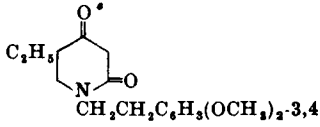
TABLE III—Continued
DIECKMANN CONDENSATIONS LEADING TO HETEROCYCLES

158

ORGANIC REACTIONS

THE DIECKMANN CONDENSATION

159

C2. Heterocycles Containing Nitrogen in a Six-Membered Ring—Continued				
Starting Ester	Product(s)	Base	Yield (%)	Refs.
<i>C₁₆ (contd.)</i>				
	<p>A</p> 	NaH	(A, 77) (B, 9)	317
	<p>B</p> 	NaOC2H5	(A, 0) (B, 31)	317
		NaOC2H5	(35)	351 349*
$\text{CH}_2\text{CH}(\text{C}_2\text{H}_5)\text{CO}_2\text{C}_2\text{H}_5$ $\text{NCH}_2\text{CH}_2\text{C}_6\text{H}_5$ $\text{CH}_2\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5$		NaH	(72)	576
$\text{CH}_3\text{CH}_2\text{CO}_2\text{CH}_3$ $\text{N}(\text{CH}_2)_4\text{C}_6\text{H}_5$ $\text{CH}_3\text{CH}_2\text{CO}_2\text{CH}_3$		NaH	(46)	512
<i>C₁₇</i>				
$\text{CH}_2\text{CH}(\text{CH}_2\text{CH}=\text{CH}_2)\text{CO}_2\text{C}_2\text{H}_5$ $\text{NCH}_2\text{CH}_2\text{C}_6\text{H}_5$ $\text{CH}_2\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5$		NaH	(72)	576
$\text{CH}_2\text{CH}(\text{C}_2\text{H}_5-n)\text{CO}_2\text{C}_2\text{H}_5$ $\text{NCH}_2\text{CH}_2\text{C}_6\text{H}_5$ $\text{CH}_2\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5$		NaH	(77)	576
$\text{CH}_2\text{CH}(\text{C}_2\text{H}_5-i)\text{CO}_2\text{C}_2\text{H}_5$ $\text{NCH}_2\text{CH}_2\text{C}_6\text{H}_5$ $\text{CH}_2\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5$		NaH	(72)	576
<i>C₁₈—C₂₂</i>				
$\text{CH}_2\text{CH}(\text{C}_2\text{H}_5)\text{CO}_2\text{C}_2\text{H}_5$ $\text{NCH}_2\text{CH}_2\text{C}_6\text{H}_5(\text{OCH}_3)_2-3,4$ $\text{COCH}_2\text{CO}_2\text{C}_2\text{H}_5$		Na	(62)	557

Note: References 231 to 583 are on pp. 197–203.

* This product was obtained after hydrolysis and decarboxylation.

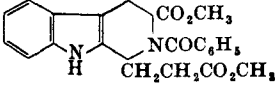
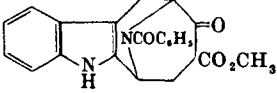
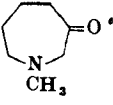
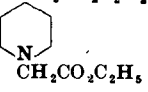
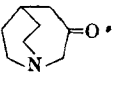
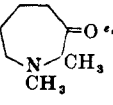
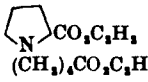
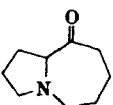
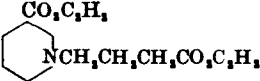
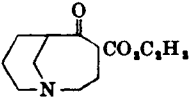
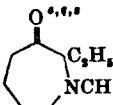
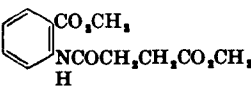
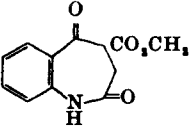
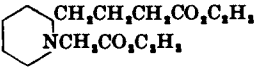
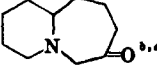
* The product was isolated as the hydrochloride.

* The carbonyl group of the β -N-propionate part of the molecule was ¹⁴C-labeled.

TABLE III—Continued
DIECKMANN CONDENSATIONS LEADING TO HETEROCYCLES

160

ORGANIC REACTIONS

C2. Heterocycles Containing Nitrogen in a Six-Membered Ring—Continued				
Starting Ester	Product(s)	Base	Yield (%)	Refs.
<i>C₁₈–C₂₂ (contd.)</i>				
		NaH	(90)	447
C3. Heterocycles Containing Nitrogen in a Seven-Membered Ring				
<i>C₉</i>				
$\text{CH}_2\text{CH}_2\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5$ $\text{CH}_2\text{N}(\text{CH}_3)\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5$		NaOC ₂ H ₅	(20)	133
<i>C₉</i>				
$\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5$ 		KOC ₄ H ₉ -t	(0.7)	330
$(\text{CH}_2)_4\text{CO}_2\text{C}_2\text{H}_5$ NCH_3 $\text{CH}(\text{CH}_3)\text{CO}_2\text{C}_2\text{H}_5$		NaOC ₂ H ₅	(46)	325
<i>C₁₀</i>				
		NaOC ₂ H ₅	(27)	327
$\text{CO}_2\text{C}_2\text{H}_5$ 		NaOC ₂ H ₅	(0)	142
$(\text{CH}_2)_4\text{CO}_2\text{C}_2\text{H}_5$ NCH_3 $\text{CH}(\text{C}_2\text{H}_5)\text{CO}_2\text{C}_2\text{H}_5$		NaOC ₂ H ₅	(52)	517
<i>C₁₁</i>				
		Na	(38)	544
		NaOC ₂ H ₅	(36)	59

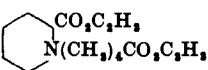
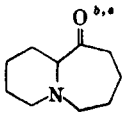
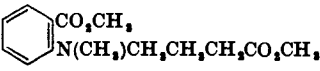
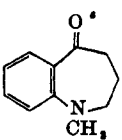
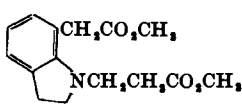
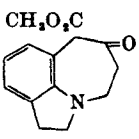
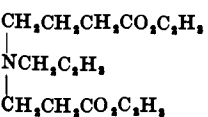
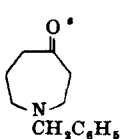
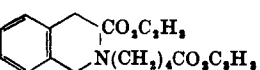
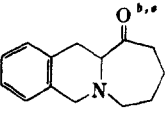
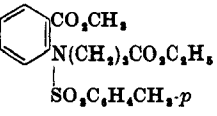
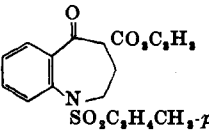
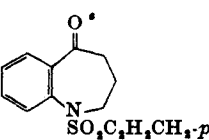
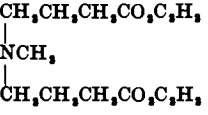
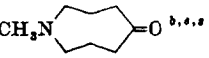
Note: References 231 to 583 are on pp. 197–203.

- * This reaction was done under high-dilution conditions.
- * This product was obtained after hydrolysis and decarboxylation.
- * Alcohol was removed by azeotropic distillation with the solvent.
- * The product was isolated as the hydrochloride.

THE DIECKMANN CONDENSATION

161

TABLE III—Continued
DIECKMANN CONDENSATIONS LEADING TO HETEROCYCLES

C3. Heterocycles Containing Nitrogen in a Seven-Membered Ring—Continued				
Starting Ester	Product(s)	Base	Yield (%)	Refs.
C ₁₁ (contd.)				
		KOC ₄ H ₉ -t	(79)	61
C ₁₂				
		KOC ₄ H ₉ -t Na NaH	(48-52) (27-48) (0)	237, 480 480 480
C ₁₃				
		KOC ₄ H ₉ -t	(55)	583
C ₁₄				
		NaOC ₄ H ₉	(20)	564
C ₁₅				
		KOC ₄ H ₉ -t	(69)	62
C ₁₆				
		KOC ₄ H ₉ -t	(Good)	234
		KOC ₄ H ₉ -t	(Low)	333
C4. Heterocycles Containing Nitrogen in an Eight-Membered Ring				
		KOC ₄ H ₉ -t	(20)	63, 64

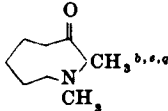


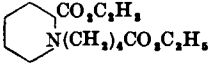
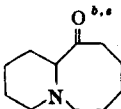

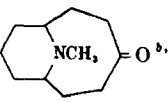
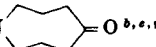

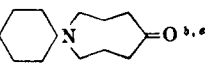
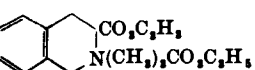
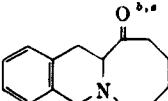
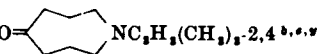
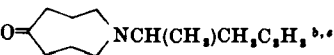

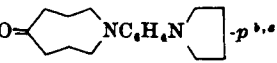
Note: References 231 to 583 are on pp. 197-203.

- ^a This reaction was done under high-dilution conditions.
- ^b This product was obtained after hydrolysis and decarboxylation.
- ^c The product was isolated as the hydrochloride.

TABLE III—Continued
DIECKMANN CONDENSATIONS LEADING TO HETEROCYCLES

164

ORGANIC REACTIONS

C4. Heterocycles Containing Nitrogen in an Eight-Membered Ring—Continued				
Starting Ester	Product(s)	Base	Yield (%)	Refs.
$(\text{CH}_3)_2\text{CO}_2\text{C}_2\text{H}_5$ NCH_3 $\text{CH}(\text{CH}_3)\text{CO}_2\text{C}_2\text{H}_5$		KOC_4H_9-t	(55)	60
$(\text{CH}_3)_2\text{CO}_2\text{C}_2\text{H}_5$  $(\text{CH}_3)_2\text{CO}_2\text{C}_2\text{H}_5$		NaH	(42)	68
		KOC_4H_9-t	(24)	61
$(\text{CH}_3)_2\text{CO}_2\text{C}_2\text{H}_5$  $(\text{CH}_3)_2\text{CO}_2\text{C}_2\text{H}_5$		KOC_4H_9-t	(23)	65
$\text{CH}_3\text{CH}_2\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5$ $\text{NC}_2\text{H}_4\text{CH}_2-p$ $\text{CH}_3\text{CH}_2\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5$	$p\text{-CH}_2\text{C}_2\text{H}_4\text{N}$ 	NaH	(64)	66
$(\text{CH}_3)_2\text{CO}_2\text{CH}_3$  $(\text{CH}_3)_2\text{CO}_2\text{CH}_3$		NaH	(45)	63
		KOC_4H_9-t	(42)	62
$\text{CH}_3\text{CH}_2\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5$ $\text{NC}_2\text{H}_4(\text{CH}_2)_3-2,4$ $\text{CH}_3\text{CH}_2\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5$		NaH	(3)	66
$\text{CH}_3\text{CH}_2\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5$ $\text{NCH}(\text{CH}_3)\text{CH}_2\text{C}_2\text{H}_5$ $\text{CH}_3\text{CH}_2\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5$		NaH	(55)	67
$\text{CH}_3\text{CH}_2\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5$ $\text{NC}_2\text{H}_4\text{N}$  $\text{CH}_3\text{CH}_2\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5$		NaH	(0.7)	66

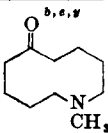
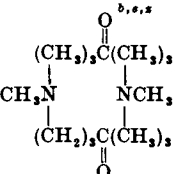
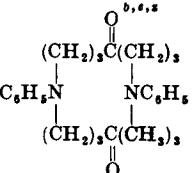
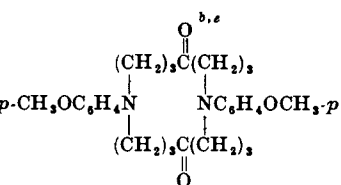
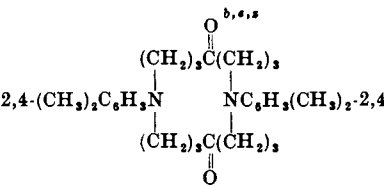
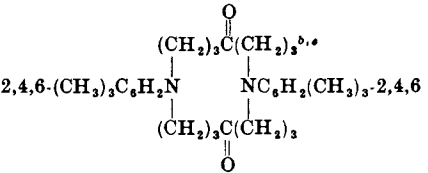
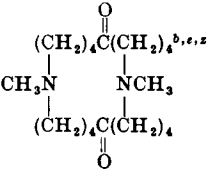
Note: References 231 to 583 are on pp. 197–203.

- ^b This reaction was done under high-dilution conditions.
- ^c This product was obtained after hydrolysis and decarboxylation.
- ^d Alcohol was removed by azeotropic distillation with the solvent.
- ^e The dimer was also formed; see below.

165

THE DIECKMANN CONDENSATION

TABLE III—Continued
DIECKMANN CONDENSATIONS LEADING TO HETEROCYCLES

C5. Heterocycles Containing Nitrogen in Nine-Membered and Larger Rings				
Starting Esters	Product(s)	Base	Yield (%)	Refs.
$(\text{CH}_3)_4\text{CO}_2\text{C}_2\text{H}_5$ NCH_3 $(\text{CH}_3)_4\text{CO}_2\text{C}_2\text{H}_5$		$\text{KOC}_4\text{H}_9\text{-}t$	(10)	63
$\text{CH}_3\text{CH}_2\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5$ NCH_3 $\text{CH}_3\text{CH}_2\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5$		$\text{KOC}_4\text{H}_9\text{-}t$	(29)	63
$\text{CH}_3\text{CH}_2\text{CH}_2\text{CO}_2\text{CH}_3$ NC_6H_5 $\text{CH}_3\text{CH}_2\text{CH}_2\text{CO}_2\text{CH}_3$		NaH	(0.4)	66
$\text{CH}_3\text{CH}_2\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5$ $\text{NC}_6\text{H}_4\text{OCH}_3\text{-}p$ $\text{CH}_3\text{CH}_2\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5$		NaH	(0.3)	66
$\text{CH}_3\text{CH}_2\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5$ $\text{NC}_6\text{H}_3(\text{CH}_3)_2\text{-}2,4$ $\text{CH}_3\text{CH}_2\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5$		NaH	(0.1)	66
$\text{CH}_3\text{CH}_2\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5$ $\text{NC}_6\text{H}_3(\text{CH}_3)_3\text{-}2,4,6$ $\text{CH}_3\text{CH}_2\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5$		NaH	(0.6)	66
$(\text{CH}_3)_4\text{CO}_2\text{C}_2\text{H}_5$ NCH_3 $(\text{CH}_3)_4\text{CO}_2\text{C}_2\text{H}_5$		$\text{KOC}_4\text{H}_9\text{-}t$	(30)	63

Note: References 231 to 583 are on pp. 197-203.

^b This reaction was done under high-dilution conditions.

^c This product was obtained after hydrolysis and decarboxylation.

^d The dimer was also formed; see below.

^e The monomer was also formed; see above.

TABLE IV
INTERMOLECULAR ESTER CONDENSATIONS FOLLOWED BY CYCLIZATION

A. Condensations Involving Two Different Esters and Leading to Carbocyclic Products				
Starting Esters	Product(s)	Base	Yield (%)	Refs.
Diethyl Oxalate* and $\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5$ $\text{COCH}_2\text{CO}_2\text{C}_2\text{H}_5$		KOC_2H_5	(85)†	474
$\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5$ $\text{CH}_2\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5$		NaOC_2H_5	(80)	240, 73
$\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5$ $\text{CHCO}_2\text{C}_2\text{H}_5$ $\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5$		NaOC_2H_5	(70-100)	74b, 416‡
$\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5$ $\text{CH}(\text{CH}_3)\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5$		NaOC_2H_5	(90-100)	240, 236, 281
$\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5$ $\text{C}(\text{CO}_2\text{C}_2\text{H}_5)_2$ $\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5$		NaOC_2H_5	(75)	74b
$\text{CH}_2\text{CO}_2\text{CH}_3$ $\text{C}(\text{CH}_3)_2\text{CH}_2\text{CO}_2\text{CH}_3$		NaOCH_3	(70)¶	75
$\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5$ $\text{C}(\text{CH}_3)_2\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5$		NaOC_2H_5	(Poor)¶	236, 313, 356
$\text{CH}_2\text{CO}_2\text{CH}_3$ $\text{CH}_3\text{CC}_2\text{H}_5$ $\text{CH}_2\text{CO}_2\text{CH}_3$		NaOCH_3	(20)	240
		NaOCH_3	(60-70)	240
$\text{CH}_2\text{CO}_2\text{CH}_3$ $\text{C}(\text{C}_2\text{H}_5)_2$ $\text{CH}_2\text{CO}_2\text{CH}_3$		NaOCH_3	(Low)	240

Note: References 231 to 583 are on pp. 197-203.

* The products of many reactions with diethyl oxalate have been formulated as dicarbethoxycyclopentadienols. All the examples in this table have been arbitrarily written in the diketo form. Where the authors specified the dienol form, the fact has been indicated in a footnote.

† The product was isolated and reported as the dipotassium salt.

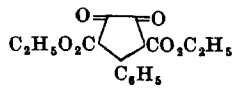
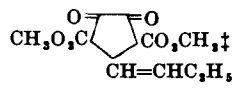
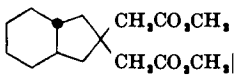
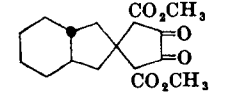
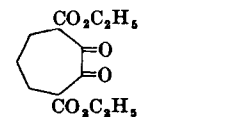
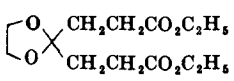
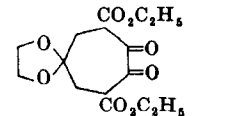
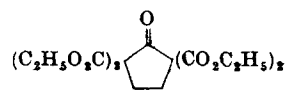
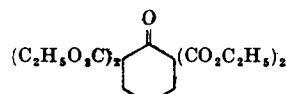
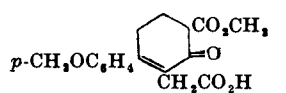
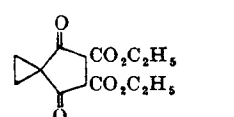
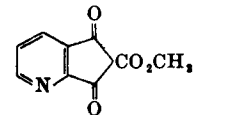
‡ The product was formulated as the dienol.

¶ Dimethyl oxalate was used in this reaction.

§ Diethyl carbonate is also formed.

¶ Six equivalents of dimethyl oxalate were used with the dimethyl α -ketoglutarate. With the ethyl esters the ratio of glutarate to oxalate was 1:1.

TABLE IV—Continued
INTERMOLECULAR ESTER CONDENSATIONS FOLLOWED BY CYCLIZATION

A. Condensations Involving Two Different Esters and Leading to Carbocyclic Products—Continued				
Starting Esters	Product(s)	Base	Yield (%)	Refs.
<i>Diethyl Oxalate (contd.) and</i>				
$\text{CH}_3\text{CO}_2\text{C}_2\text{H}_5$ CHC_2H_5 $\text{CH}_3\text{CO}_2\text{CH}_3$		NaOC_2H_5	(Good)	236, 282†
$\text{CH}_3\text{CO}_2\text{CH}_3$ $\text{CHCH}=\text{CHC}_2\text{H}_5$ $\text{CH}_3\text{CO}_2\text{CH}_3$		NaOCH_3	(—)	282
		NaOCH_3	(50)	280
$\text{CH}_3\text{CO}_2\text{C}_2\text{H}_5$ $(\text{CH}_2)_6$ $\text{CH}_3\text{CO}_2\text{C}_2\text{H}_5$		NaOC_2H_5	(—)	465
		NaOC_2H_5	(21)	76
<i>Carbonyl Bromide and</i>				
$\text{CH}_2\text{CH}(\text{CO}_2\text{C}_2\text{H}_5)_2$ $\text{CH}_2\text{CH}(\text{CO}_2\text{C}_2\text{H}_5)_2$		Na	(35)	27
$\text{CH}_3\text{CH}_2\text{CH}(\text{CO}_2\text{C}_2\text{H}_5)_2$ $\text{CH}_2\text{CH}(\text{CO}_2\text{C}_2\text{H}_5)_2$		Na	(Good)	27
<i>Dimethyl Succinate and</i>				
$\text{COC}_6\text{H}_4\text{OCH}_3 \cdot p$ $\text{CH}_2\text{CH}_2\text{CH}_2\text{CO}_2\text{CH}_3$		NaH $\text{KOC}_2\text{H}_5 \cdot t$	(58) (49)	279 279
<i>Diethyl 1,1-Cyclopropanedicarboxylate and</i>				
$\text{CH}_3\text{CO}_2\text{C}_2\text{H}_5$ $\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5$		NaNH_2	(Low)	471
<i>Dimethyl 2,3-Pyridinedicarboxylate and</i>				
Methyl acetate		Na	(—)	470

Note: References 231 to 583 are on pp. 197–203.

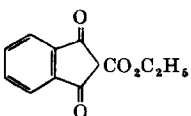
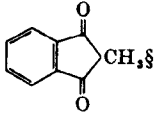
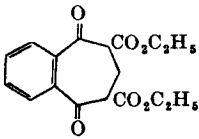
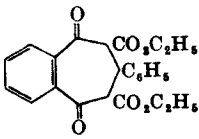
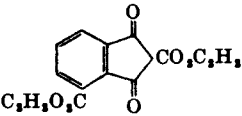
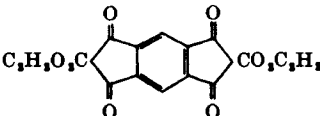
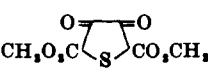
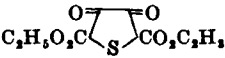
† The product was formulated as the dienol.

|| Dimethyl oxalate was used in this reaction.

TABLE IV—Continued
INTERMOLECULAR ESTER CONDENSATIONS FOLLOWED BY CYCLIZATION

172

ORGANIC REACTIONS

A. Condensations Involving Two Different Esters and Leading to Carbocyclic Products—Continued				
Starting Esters	Product(s)	Base	Yield (%)	Refs.
<i>Diethyl Phthalate and</i>				
Ethyl acetate		NaOC ₂ H ₅	(Good)	347
Ethyl propionate		Na	(—)	348
CH ₃ CO ₂ C ₂ H ₅ CH ₂ CH ₂ CO ₂ C ₂ H ₅		Na	(50)	77
CH ₃ CO ₂ C ₂ H ₅ CHC ₆ H ₅ CH ₂ CO ₂ C ₂ H ₅		Na	(—)	77
<i>Triethyl Hemimellitate and</i>				
Ethyl acetate		Na	(—)	246
<i>Tetraethyl Pyromellitate and</i>				
Ethyl acetate		Na	(—)	239
B. Condensations Involving Two Different Esters and Leading to Heterocyclic Products				
<i>Diethyl Oxalate* and</i>				
CH ₃ CO ₂ CH ₃ S CH ₃ CO ₂ CH ₃ CH ₃ CO ₂ C ₂ H ₅ S CH ₃ CO ₂ C ₂ H ₅		NaOCH ₃	(59)	265, ‡ 373
		NaOC ₂ H ₅	(—)	265 ‡

Note: References 231 to 583 are on pp. 197–203.

* The products of many reactions with diethyl oxalate have been formulated as dicarbethoxycyclopentadienols. All the examples in this table have been arbitrarily written in the diketo form. Where the authors specified the dienol form, the fact has been indicated in a footnote.

‡ The product was formulated as the dienol.

§ Diethyl carbonate is also formed.

|| Dimethyl oxalate was used in this reaction.

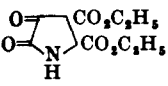
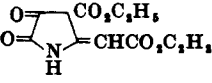

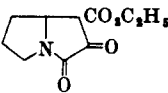
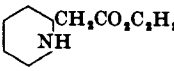
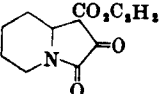


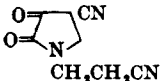
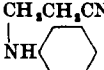
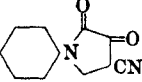

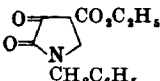
THE DIECKMANN CONDENSATION

173

TABLE IV—Continued
INTERMOLECULAR ESTER CONDENSATIONS FOLLOWED BY CYCLIZATION

174

ORGANIC REACTIONS

B. Condensations Involving Two Different Esters and Leading to Heterocyclic Products—Continued				
Starting Esters	Product(s)	Base	Yield (%)	Refs.
<i>Diethyl Oxalate (contd.) and</i>				
$\begin{array}{c} \text{CH}_2\text{CO}_2\text{C}_2\text{H}_5 \\ \\ \text{CH}(\text{NH}_2)\text{CO}_2\text{C}_2\text{H}_5 \end{array}$		NaOC_2H_5	(94)	79
$\begin{array}{c} \text{CH}_2\text{CO}_2\text{C}_2\text{H}_5 \\ \\ \text{C}=\text{CHCO}_2\text{C}_2\text{H}_5 \\ \\ \text{NH}_2 \end{array}$		NaOC_2H_5	(92)	79
		NaOC_2H_5	(82)	79
		NaOC_2H_5	(70)	79
$\begin{array}{c} \text{CH}_2\text{CH}_2\text{CN} \\ \\ \text{NHCH}_3 \end{array}$		NaOCH_3 NaOC_2H_5	(81) (75)	79 79
$\begin{array}{c} \text{CH}_2\text{CH}_2\text{CN} \\ \\ \text{NHC}_2\text{H}_5 \end{array}$		NaOCH_3	(67)	79
$\begin{array}{c} \text{CH}_2\text{CH}_2\text{CN} \\ \\ \text{NHCH}_2\text{CH}_2\text{CN} \end{array}$		NaOCH_3 NaOC_2H_5	(41) (58)	79 79
		NaOC_2H_5	(66)	79
$\begin{array}{c} \text{CH}_2\text{CH}_2\text{CN} \\ \\ \text{NHCH}_2\text{C}_6\text{H}_5 \end{array}$		NaOC_2H_5	(70)	79
$\begin{array}{c} \text{CH}_2\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5 \\ \\ \text{NCH}_2\text{C}_6\text{H}_5 \\ \\ \text{CH}_2\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5 \end{array}$		NaOC_2H_5	(46)	380

Note: References 231 to 583 are on pp. 197–203.

|| Dimethyl oxalate was used in this reaction.

THE DIECKMANN CONDENSATION

175

TABLE IV—Continued
INTERMOLECULAR ESTER CONDENSATIONS FOLLOWED BY CYCLIZATION

176

ORGANIC REACTIONS

B. Condensations Involving Two Different Esters and Leading to Heterocyclic Products—Continued				
Starting Esters	Product(s)	Base	Yield (%)	Refs.
<i>Diethyl Succinate and</i>				
		NaH	(30)	78
C. Self-Condensations**				
<i>o</i> -ClC ₆ H ₄ CH=CHCO ₂ C ₂ H ₅		Na	(9)	69
<i>p</i> -ClC ₆ H ₄ CH=CHCO ₂ C ₂ H ₅		Na	(9)	69
C ₆ H ₅ CH=CHCO ₂ C ₂ H ₅		Na	(22)	70, 69, †† 71
<i>p</i> -CH ₃ C ₆ H ₄ CH=CHCO ₂ C ₂ H ₅		Na	(25)	69
CH ₃ (CO ₂ C ₂ H ₅) ₂		Na	(—)	284
		Na	(55)	464 §§
		NaOC ₂ H ₅ Na	(Good) (30–75)	2, 3, 368 4–7, 464 §§
		Na	(—)	464 §§

Note: References 231 to 583 are on pp. 197–203.

** The list of references for diethyl succinate dimerization is representative, not exhaustive. Dimerizations of esters other than succinic esters are listed in Tables II and III under the appropriate ring size.

†† A prior reduction to diethyl 3,4-diphenyladipate is involved.

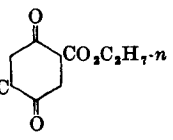
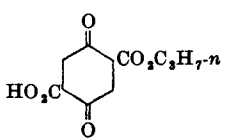
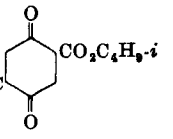
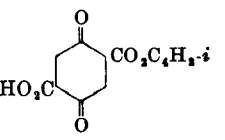
‡‡ The authors of Ref. 69 also studied the effect on the yield of changing the ester group.

§§ The solvent was the acetic acid ester corresponding to the alcohol in the succinate.

THE DIECKMANN CONDENSATION

177

TABLE IV—Continued
INTERMOLECULAR ESTER CONDENSATIONS FOLLOWED BY CYCLIZATION

C. Self-Condensations—Continued				
Starting Ester	Product(s)	Base	Yield (%)	Refs.
$\begin{array}{c} \text{CH}_2\text{CO}_2\text{C}_3\text{H}_7\cdot n \\ \\ \text{CH}_2\text{CO}_2\text{C}_3\text{H}_7\cdot n \end{array}$	<p>A </p>	Na	(A, 64) (B, 18)	464 §§
	<p>B </p>			
$\begin{array}{c} \text{CH}_2\text{CO}_2\text{C}_4\text{H}_9\cdot i \\ \\ \text{CH}_2\text{CO}_2\text{C}_4\text{H}_9\cdot i \end{array}$	<p>A </p>	Na	(A, 44) (B, 19)	464 §§
	<p>B </p>			

Note: References 231 to 583 are on pp. 197–203.

§§ The solvent was the acetic acid ester corresponding to the alcohol in the succinate.

TABLE V
MICHAEL CONDENSATIONS FOLLOWED BY CYCLIZATION*

A. Reactions Leading to Carbocyclic Products				
Starting Esters	Product(s)	Base	Yield (%)	Refs.
$\text{cis } \begin{array}{c} \text{CH}_3\text{CCO}_2\text{C}_2\text{H}_5 \\ \parallel \\ \text{CHCO}_2\text{C}_2\text{H}_5 \end{array}$ and $\text{CH}_3(\text{CO}_2\text{C}_2\text{H}_5)_2$	$\begin{array}{c} \text{C}_2\text{H}_5\text{O}_2\text{C} \diagup \text{O} \uparrow \\ \text{C}_2\text{H}_5\text{O}_2\text{C} \diagdown \text{CH}_2 \\ \text{CH}_2 \end{array}$	NaOC_2H_5	(—)	82
	$\begin{array}{c} \text{O} \\ \parallel \\ \text{C}_2\text{H}_5\text{O}_2\text{C} \diagup \text{Cyclopentane} \diagdown \text{CO}_2\text{C}_2\text{H}_5 \\ \parallel \\ \text{CO}_2\text{C}_2\text{H}_5 \end{array}$	NaOC_2H_5	(Low)	84, 85
$\text{C}_2\text{H}_5\text{CH}(\text{CO}_2\text{C}_2\text{H}_5)_2$	$\begin{array}{c} \text{C}_2\text{H}_5 \\ \parallel \\ \text{O} \diagup \text{Cyclopentane} \diagdown \text{CO}_2\text{C}_2\text{H}_5 \\ \parallel \\ \text{C}_2\text{H}_5\text{O}_2\text{C} \text{CH}_2 \\ \parallel \\ \text{CO}_2\text{C}_2\text{H}_5 \end{array}$	NaOC_2H_5	(45)	82
$\text{CH}_2=\text{CCO}_2\text{C}_2\text{H}_5$ and $\begin{array}{c} \text{CH}_2\text{CO}_2\text{C}_2\text{H}_5 \\ \\ \text{NaC}(\text{CH}_3)\text{CO}_2\text{C}_2\text{H}_5 \\ \\ \text{CO}_2\text{C}_2\text{H}_5 \end{array}$	$\begin{array}{c} \text{O} \\ \parallel \\ \text{C}_2\text{H}_5\text{O}_2\text{C} \diagup \text{Cyclopentane} \diagdown \text{CO}_2\text{C}_2\text{H}_5 \\ \parallel \\ \text{C}_2\text{H}_5\text{O}_2\text{C} \text{CH}_2 \end{array}$	—	(—)	86

Note: References 231 to 583 are on pp. 197–203.

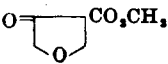
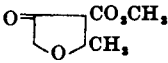
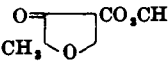
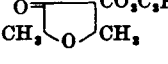
* The α,β -unsaturated esters are *trans* unless otherwise indicated.

† These are the structures given in the reference cited. They are almost certainly incorrect. Citraconate is known to isomerize to itaconate, and the products are cyclopentanones; see examples immediately following. Several other examples are also reported.

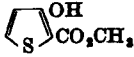
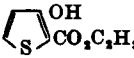
TABLE V—Continued
MICHAEL CONDENSATIONS FOLLOWED BY CYCLIZATION*

A. Reactions Leading to Carbocyclic Products—Continued				
Starting Esters	Product(s)	Base	Yield (%)	Refs.
$\text{CH}_2=\text{CHCO}_2\text{CH}_3$ and				
$\begin{array}{c} \text{CH}_2\text{CHCO}_2\text{C}_2\text{H}_5 \\ \\ \text{CH}(\text{CO}_2\text{C}_2\text{H}_5)_2 \end{array}$	<p>A</p> $\begin{array}{c} \text{O} \\ \parallel \\ \text{CH}_3 \\ \diagup \text{Cyclopentane} \diagdown \text{CO}_2\text{C}_2\text{H}_5 \\ \parallel \\ (\text{CO}_2\text{C}_2\text{H}_5)_2 \end{array}$	NaOC_2H_5	(A + B, 61–67)	427
	<p>B</p> $\begin{array}{c} \text{O} \\ \parallel \\ \text{CH}_3 \\ \diagup \text{Cyclopentane} \diagdown \text{CO}_2\text{C}_2\text{H}_5 \\ \parallel \\ (\text{C}_2\text{H}_5\text{O}_2\text{C})_2 \end{array}$			
$\begin{array}{c} \text{CHCH}_2\text{CO}_2\text{C}_2\text{H}_5 \\ \parallel \\ \text{CHCH}_2\text{CO}_2\text{C}_2\text{H}_5 \end{array}$ and				
$\text{CH}_3(\text{CO}_2\text{C}_2\text{H}_5)_2$	$\begin{array}{c} \text{O} \\ \parallel \\ \text{C}_2\text{H}_5\text{O}_2\text{C} \diagup \text{Cyclopentane} \diagdown \text{CO}_2\text{C}_2\text{H}_5 \\ \parallel \\ \text{CH}_2\text{CO}_2\text{C}_2\text{H}_5 \end{array}$	NaOC_2H_5	(25)	248
$\text{CH}_2=\text{C}(\text{CO}_2\text{CH}_3)_2$ and				
$\begin{array}{c} \text{CH}_2\text{CH}_2\text{CO}_2\text{CH}_3 \\ \\ \text{CH}_2\text{CO}_2\text{CH}_3 \end{array}$	$\begin{array}{c} \text{CO}_2\text{CH}_3 \\ \parallel \\ \text{CH}_2\text{O}_2\text{C} \diagup \text{Cyclohexane} \diagdown \text{CO}_2\text{CH}_3 \\ \parallel \\ \text{O} \text{Cyclohexane} \text{CO}_2\text{CH}_3 \\ \parallel \\ \text{CO}_2\text{CH}_3 \end{array}$	NaOCH_3	(66)	91, 92

B. Reactions Leading to Oxygen Heterocycles

Methyl Glycolate and $\text{CH}_2=\text{CHCO}_2\text{CH}_3$		Na	(46)	218
$\text{CH}_3\text{CH}=\text{CHCO}_2\text{CH}_3$		NaH	(65)	218
$\text{CH}_3\text{CHOHCO}_2\text{CH}_3$ and $\text{CH}_2=\text{CHCO}_2\text{CH}_3$		NaH	(58)	218
$\text{CH}_3\text{CHOHCO}_2\text{C}_2\text{H}_5$ and $\text{CH}_3\text{CH}=\text{CHCO}_2\text{C}_2\text{H}_5$		NaH	(40)	87

C. Reactions Leading to Sulfur Heterocycles

Methyl Thioglycolate and $\text{HC}\equiv\text{CCO}_2\text{CH}_3$		NaOCH_3	(28)	81
		NaOC_2H_5	(30)§	81

Note: References 231 to 583 are on pp. 197-203.

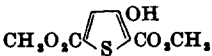
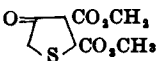
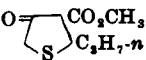
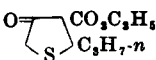
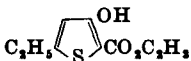
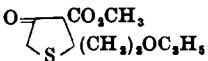
* The α,β -unsaturated esters are *trans* unless otherwise indicated.

† Prior isomerization to an α,β -unsaturated ester is required.

§ The ethyl ester of thioglycolic acid was used.

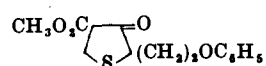
TABLE V—Continued
MICHAEL CONDENSATIONS FOLLOWED BY CYCLIZATION*

C. Reactions Leading to Sulfur Heterocycles—Continued

Starting Esters	Product(s)	Base	Yield (%)	Refs.
Methyl Thioglycolate (contd.) and $\text{CH}_3\text{O}_2\text{C}\equiv\text{CCO}_2\text{CH}_3$		NaOCH_3	(94)	80
<i>cis</i> $\begin{array}{c} \text{CHCO}_2\text{CH}_3 \\ \parallel \\ \text{CHCO}_2\text{CH}_3 \end{array}$		NaOCH_3	(38)	80
CHCO_2CH_3 \parallel $\text{CHC}_2\text{H}_{7-n}$		NaOCH_3	(52)	285
$\text{CHCO}_2\text{C}_2\text{H}_5$ § \parallel $\text{CHC}_2\text{H}_{7-n}$		NaOC_2H_5	(66)	285
$\text{C}_6\text{H}_5\text{C}\equiv\text{CCO}_2\text{C}_2\text{H}_5$ §		NaOC_2H_5	(30)	81
CHCO_2CH_3 \parallel $\text{CH}(\text{CH}_3)_2\text{OC}_2\text{H}_5$		NaOCH_3	(72)	285

$C_2H_5O(CH_2)_3CHSHCO_2CH_3$ and

$CH_2=CHCO_2CH_3$



$NaOCH_3$

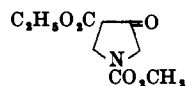
(73)

285

D. Reactions Leading to Nitrogen Heterocycles

Ethyl Acrylate and

$CH_2CO_2C_2H_5$
|
 $NHCO_2CH_3$

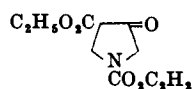


NaH

(53)

88

$CH_2CO_2C_2H_5$
|
 $NHCO_2C_2H_5$



NaH

(78)

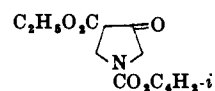
88

Na

(72)

89

$CH_2CO_2C_2H_5$
|
 $NHCO_2C_2H_5$

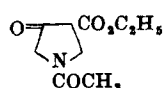


NaH

(65)

88

$CH_2CO_2C_2H_5$
|
 $NHCOCH_3$



NaH

(57)

90

Note: References 231 to 583 are on pp. 197-203.

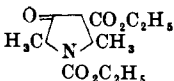
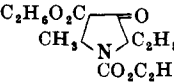
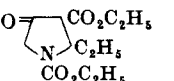
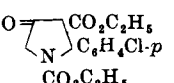
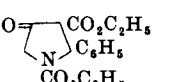
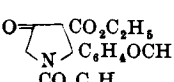
* The α,β -unsaturated esters are *trans* unless otherwise indicated.

§ The ethyl ester of thioglycolic acid was used.

TABLE V—Continued
MICHAEL CONDENSATIONS FOLLOWED BY CYCLIZATION*

D. Reactions Leading to Nitrogen Heterocycles—Continued

Starting Esters	Product(s)	Base	Yield (%)	Refs.
<i>Ethyl Acrylate (contd.) and</i>				
$CH(CH_3)CO_2C_2H_5$ $NHCO_2C_2H_5$		NaH	(68)	88
$CH(CH_3)CO_2C_2H_5$ $NHCOCH_3$		NaH	(62)	90
$CH(C_2H_5)CO_2C_2H_5$ $NHCO_2C_2H_5$		NaH	(67)	88
<i>Diethyl Fumarate and</i>				
$CH_2CO_2C_2H_5$ $NHCO_2C_2H_5$		Na	(45)	89
<i>Ethyl Crotonate and</i>				
$CH_2CO_2C_2H_5$ $NHCO_2C_2H_5$		Na	(65)	89
		NaH	(79)	88

$\begin{array}{c} \text{CH}(\text{CH}_3)\text{CO}_2\text{C}_2\text{H}_5 \\ \\ \text{NHCO}_2\text{C}_2\text{H}_5 \end{array}$		NaH	(64)	88
$\begin{array}{c} \text{CH}(\text{C}_2\text{H}_5)\text{CO}_2\text{C}_2\text{H}_5 \\ \\ \text{NHCO}_2\text{C}_2\text{H}_5 \end{array}$		NaH	(50)	88
$\text{C}_2\text{H}_5\text{CH}=\text{CHCO}_2\text{C}_2\text{H}_5$ and				
$\begin{array}{c} \text{CH}_2\text{CO}_2\text{C}_2\text{H}_5 \\ \\ \text{NHCO}_2\text{C}_2\text{H}_5 \end{array}$		NaH	(53)	88
$p\text{-ClC}_6\text{H}_4\text{CH}=\text{CHCO}_2\text{C}_2\text{H}_5$ and				
$\begin{array}{c} \text{CH}_2\text{CO}_2\text{C}_2\text{H}_5 \\ \\ \text{NHCO}_2\text{C}_2\text{H}_5 \end{array}$		NaH	(18)	88
$\text{C}_6\text{H}_5\text{CH}=\text{CHCO}_2\text{C}_2\text{H}_5$ and				
$\begin{array}{c} \text{CH}_2\text{CO}_2\text{C}_2\text{H}_5 \\ \\ \text{NHCO}_2\text{C}_2\text{H}_5 \end{array}$		NaH Na	(33) (39)	88 89
$p\text{-CH}_3\text{OC}_6\text{H}_4\text{CH}=\text{CHCO}_2\text{C}_2\text{H}_5$ and				
$\begin{array}{c} \text{CH}_3\text{CO}_2\text{C}_2\text{H}_5 \\ \\ \text{NHCO}_2\text{C}_2\text{H}_5 \end{array}$		NaH	(21)	88

Note: References 231 to 583 are on pp. 197-203.

* The α,β -unsaturated esters are *trans* unless otherwise indicated.

TABLE VI
THORPE-ZIEGLER CONDENSATIONS
(All the products are written as enamines. See pp. 28-29.)

A. Reactions Leading to Five-Membered Rings				
Starting Nitrile	Product(s)	Base	Yield (%)	References
$\text{CH}_3\text{CH}_2\text{CN}$ $\text{CH}_3\text{CH}_2\text{CN}$	A	NaOC_2H_5 $t\text{-C}_4\text{H}_9\text{NHMgBr}$ NaOC_2H_5 - t in toluene	(A, 0-84) ^a (A, 49) (A, 85) ^b	162, 155, 156 156, 354 156
	B	NaOC_2H_5 - t in $t\text{-C}_4\text{H}_9\text{OH}$ NaOC_2H_5	(A, 5) ^c (B, 67-76) (A, 39) ^d (B, 25)	156 156
		NaOC_2H_5 in $\text{CO}(\text{OC}_2\text{H}_5)_2$	(53)	158
$\text{CH}_3\text{CH}(\text{CN})\text{CO}_2\text{C}_2\text{H}_5$ $\text{CH}_3\text{CH}(\text{CN})\text{CO}_2\text{C}_2\text{H}_5$		NaOC_2H_5	(35)	158, 163, 381*
		NaH	(78)	157
$\text{CH}_3\text{C}(\text{CH}_3)_2\text{CN}$ $\text{CH}_3\text{CH}_2\text{CN}$		NaNH_2	(67)	177
		NaOC_2H_5	(Quant.)	154
		NaH	(74)	157
		NaH	(93)	157
		NaH	(85)	157
		NaOC_2H_5 $\text{NaOCH}_2\text{CH}_2\text{OH}$	(0) (75)	554 554

Note: References 231 to 583 are on pp. 197-203.

* An incorrect structure was written by the authors; cf. ref. 163.

^a In reference 162 a trace of sodium ethoxide in ethanol was used. In reference 150, 0.2 equivalent of ethoxide was used and 94% recovery of starting material was reported.

^b Heterogeneous conditions and an equivalent of base were used.

^c The reaction was run under homogeneous conditions with a catalytic amount of base.

^d These are yields for reaction with one equivalent of base after one hour at reflux; 35% of starting material was also recovered. After 20 hours at reflux a mixture of A and B only was obtained.

^e The starting material was prepared *in situ* from ethylene dibromide and ethyl cyanoacetate.

^f The nitrile was prepared *in situ* in dimethyl sulfoxide from *bis*-1,2-bromomethylcyclobutane and sodium cyanide.

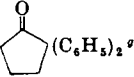
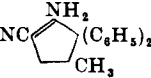
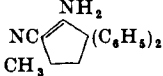
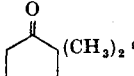
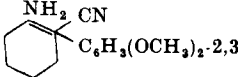
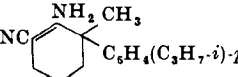
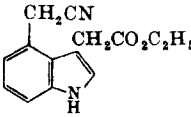
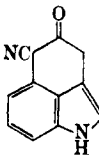
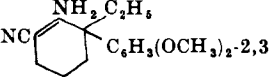
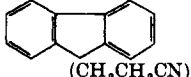
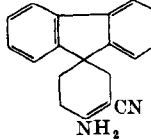
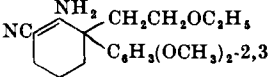
^g The intermediate was hydrolyzed and decarboxylated.

^h The nitrile was prepared *in situ* in dimethyl sulfoxide from the appropriate ditoluenesulfonate and sodium cyanide.

TABLE VI—Continued
THORPE-ZIEGLER CONDENSATIONS

188

ORGANIC REACTIONS

A. Reactions Leading to Five-Membered Rings—Continued				
Starting Nitrile	Product(s)	Base	Yield (%)	References
$\text{C}(\text{C}_6\text{H}_5)_2\text{CN}$ $\text{CH}_2\text{CH}_2\text{CH}_2\text{CN}$	 $(\text{C}_6\text{H}_5)_2\text{C}^{\text{a}}$	$\text{NaOC}_4\text{H}_9\text{-}t^{\text{b}}$ NaOC_2H_5 NaNH_2	(81) (0) (50)	415 415 415
$\text{C}(\text{C}_6\text{H}_5)_2\text{CN}$ $\text{CH}(\text{CH}_3)\text{CH}_2\text{CH}_2\text{CN}$	 $(\text{C}_6\text{H}_5)_2\text{C}^{\text{a}}$	$\text{NaOC}_4\text{H}_9\text{-}t^{\text{b}}$ NaNH_2^{c}	(Good) (9)	414 414
$\text{C}(\text{C}_6\text{H}_5)_2\text{CN}$ $\text{CH}_2\text{CH}(\text{CH}_3)\text{CH}_2\text{CN}$	 $(\text{C}_6\text{H}_5)_2\text{C}^{\text{a}}$	$\text{NaOC}_4\text{H}_9\text{-}t^{\text{b}}$	(Good)	414
B. Reactions Leading to Six-Membered Rings				
$\text{CH}_2\text{C}(\text{CH}_3)_2\text{CN}$ $\text{CH}_2\text{CH}_2\text{CH}_2\text{CN}$	 $(\text{CH}_3)_2\text{C}^{\text{a}}$	NaNH_2	(—)	177
$\text{CH}(\text{CN})\text{C}_6\text{H}_3(\text{OCH}_3)_2\text{-}2,3$ $\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CN}$	 $\text{C}_6\text{H}_3(\text{OCH}_3)_2\text{-}2,3$	Na, K	(50)	395
$p\text{-(}i\text{-C}_3\text{H}_7\text{)C}_6\text{H}_4\text{C}(\text{CH}_3)_2\text{CN}$ $\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CN}$	 $\text{C}_6\text{H}_4(\text{C}_3\text{H}_7\text{-}i)\text{-}p$	NaNH_2	(70)	390
 $\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5$		NaH	(75)	149
CN $\text{C}(\text{C}_2\text{H}_5)_2\text{C}_6\text{H}_3(\text{OCH}_3)_2\text{-}2,3$ $\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CN}$	 $\text{C}_6\text{H}_3(\text{OCH}_3)_2\text{-}2,3$	NaNH_2	(53–58)	388, 386
 $(\text{CH}_2\text{CH}_2\text{CN})_2$	 NH_2	$\text{KOC}_4\text{H}_9\text{-}t$ Na, K	(77) (80)	160 511
CN $\text{C}(\text{CH}_2\text{CH}_2\text{OC}_2\text{H}_5)_2\text{C}_6\text{H}_3(\text{OCH}_3)_2\text{-}2,3$ $\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CN}$	 $\text{CH}_2\text{CH}_2\text{OC}_2\text{H}_5$ $\text{C}_6\text{H}_3(\text{OCH}_3)_2\text{-}2,3$	NaNH_2	(55)	394

Note: References 231 to 583 are on pp. 197–203.

^a The intermediate was hydrolyzed and decarboxylated.

^b A catalytic amount of base was employed.

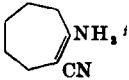
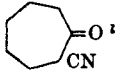
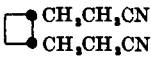
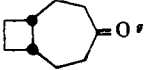

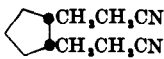
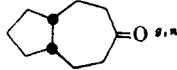
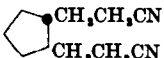
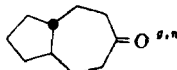
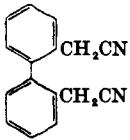
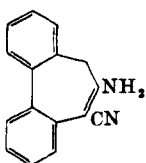
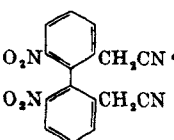
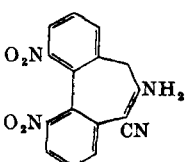
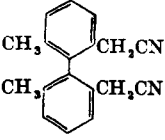
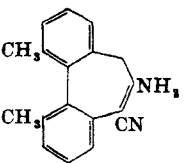
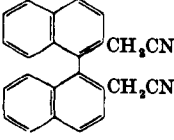
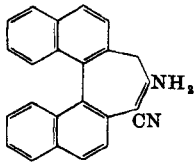
189

THE DIECKMANN CONDENSATION

TABLE VI—Continued
THORPE-ZIEGLER CONDENSATIONS

180

ORGANIC REACTIONS

C. Reactions Leading to Seven-Membered Rings				
Starting Nitrile	Product(s)	Base	Yield (%)	References
$\text{CH}_3\text{CH}_2\text{CH}_2\text{CN}$ $\text{CH}_3\text{CH}_2\text{CH}_2\text{CN}$		$\text{LiN}(\text{C}_2\text{H}_5)_3$ $\text{C}_2\text{H}_5\text{N}(\text{R})\text{Na}^{\ddagger}$	(—) (91)	354 168
		$\text{LiN}(\text{C}_2\text{H}_5)_3$ $\text{LiN}(\text{C}_2\text{H}_5)_2$ $\text{C}_2\text{H}_5\text{N}(\text{C}_2\text{H}_5)\text{Li}$	(13) ^m (71) ^j (90) ^j	165 165 165
		$\text{C}_2\text{H}_5\text{N}(\text{CH}_3)\text{Li}$	(72) ^j	47
$\text{CH}(\text{OCH}_3)\text{CH}_2\text{CH}_2\text{CN}$ $\text{CH}(\text{OCH}_3)\text{CH}_2\text{CH}_2\text{CN}$		$\text{C}_2\text{H}_5\text{N}(\text{CH}_3)\text{Li}$	(57) ^j	138
		$\text{C}_2\text{H}_5\text{N}(\text{CH}_3)\text{Li}$	(58) ^j	553
		$\text{C}_2\text{H}_5\text{N}(\text{CH}_3)\text{Li}$	(48) ^j	553
		NaOC_2H_5	(80)	412
		Aqueous-alcoholic KCN	(61)	409
		NaOC_2H_5	(66)	409
		NaOC_2H_5	(68)	410

Note: References 231 to 583 are on pp. 197–203.

^j The intermediate was hydrolyzed and decarboxylated.

^j The cyclization was carried out under high-dilution conditions.

^k The aniline base was described only as a sodium (or lithium) alkyl aniline. A later reference (171) suggests that R is methyl.

^l Partial hydrolysis occurred during the isolation of this product.

^m The cyclization was carried out in concentrated solution.

ⁿ The product was isolated as the semicarbazone derivative.

^o The nitrile was prepared *in situ* from the dibromide.

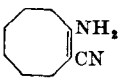
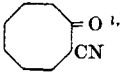

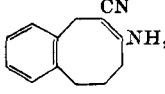
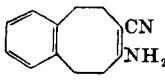
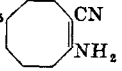
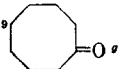
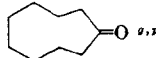
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
THE DIECKMANN CONDENSATION

TABLE VI—Continued
THORPE-ZIEGLER CONDENSATIONS

192

ORGANIC REACTIONS

D. Reactions Leading to Eight- and Nine-Membered Rings				
Starting Nitrile	Product(s)	Base	Yield (%)	References
$\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CN}$ $\text{CH}_2\text{CH}_2\text{CH}_2\text{CN}$		$\text{C}_6\text{H}_5\text{N(R)Na}^k$	(89) ^j	168
		$\text{C}_6\text{H}_5\text{N(C}_2\text{H}_5\text{)Li}$	(30) ^j	165, 354
 $\text{CH}_2\text{CH}_2\text{CN}$ $\text{CH}_2\text{CH}_2\text{CH}_2\text{CN}$	A 	$\text{C}_6\text{H}_5\text{N(CH}_3\text{)Na}$	(A, 51) (B, 20)	413
	B 			
$\text{CH(C}_6\text{H}_5\text{)CH}_2\text{CH}_2\text{CH}_2\text{CN}$ $\text{CH}_2\text{CH}_2\text{CH}_2\text{CN}$	C_6H_5 	$\text{C}_6\text{H}_5\text{N(CH}_3\text{)Na}$	(55) ^j (33) ^m	161 161
$\text{CH(C}_6\text{H}_5\text{-}t\text{)CH}_2\text{CH}_2\text{CH}_2\text{CN}$ $\text{CH}_2\text{CH}_2\text{CH}_2\text{CN}$	$t\text{-C}_4\text{H}_9$ 	$\text{C}_6\text{H}_5\text{N(CH}_3\text{)Li}$	(77) ^j	399
$\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CN}$ $\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CN}$		$\text{C}_6\text{H}_5\text{N(R)Na}^k$	(2.8) ^j	168

E. Reactions Leading to Ten-Membered and Larger Rings				
$\text{NC(CH}_2\text{)}_8\text{CN}$	Cyclodecanone ^{a,p}	$\text{C}_6\text{H}_5\text{N(R)Na}^k$	(0.37) ^j	168
$\text{NC(CH}_2\text{)}_{10}\text{CN}$	Cycloundecanone ^{a,p}	$\text{C}_6\text{H}_5\text{N(R)Na}^k$	(1.35) ^j	168
$\text{NC(CH}_2\text{)}_{11}\text{CN}$	Cyclododecanone ^{a,p}	$\text{C}_6\text{H}_5\text{N(R)Na}^k$	(8) ^j	168
$\text{NC(CH}_2\text{)}_{12}\text{CN}$	Cyclotridecanone ^{a,p}	$\text{C}_6\text{H}_5\text{N(R)Na}^k$	(15) ^j	168
$\text{NC(CH}_2\text{)}_{13}\text{CN}$	Cyclotetradecanone ^{a,q}	$\text{C}_6\text{H}_5\text{N(R)Na}^k$	(62) ^j	168
$\text{NC(CH}_2\text{)}_{14}\text{CN}$	Cyclopentadecanone ^a	$\text{C}_6\text{H}_5\text{N(R)Na}^k$	(60) ^j	168
$\text{NC(CH}_2\text{)}_{15}\text{CH(CH}_3\text{)CH}_2\text{CN}$	Muscone ^a	$\text{C}_6\text{H}_5\text{N(C}_2\text{H}_5\text{)Li}$	(44) ^{j,p}	165
$\text{NC(CH}_2\text{)}_{17}\text{CN}$	2,10-Dicyanocyclohexadecane-1,9-dione ^{t,r}	$\text{C}_6\text{H}_5\text{N(C}_2\text{H}_5\text{)Li}$	(54) ^j	167
$\text{NC(CH}_2\text{)}_{18}\text{CN}$	Cyclohexadecanone ^a	$\text{C}_6\text{H}_5\text{N(R)Na}^k$	(13) ^j	165
			(77) ^j	168
 $\text{CH}_2\text{CH}_2\text{CN}$ $\text{NC(CH}_2\text{)}_{16}\text{CN}$	Dimer	$\text{C}_6\text{H}_5\text{N(R)Na}^k$	(20) ^j	166
	Cycloheptadecanone ^a	$\text{C}_6\text{H}_5\text{N(R)Na}^k$	(70) ^j	168
		$\text{C}_6\text{H}_5\text{N(C}_2\text{H}_5\text{)Li}$	(52) ^{j,p}	165
$\text{NC(CH}_2\text{)}_{17}\text{CN}$	2-Cyanocycloheptadecanonimine	$\text{C}_6\text{H}_5\text{N(R)Na}^k$	(80) ^j	169
$\text{NC(CH}_2\text{)}_8\text{CN}$	Cyclooctadecanone ^a	$\text{C}_6\text{H}_5\text{N(R)Na}^k$	(82) ^j	168
$\text{NC(CH}_2\text{)}_{10}\text{CN}$	Cyclooctadecane-1,10-dione ^{a,q,r}	$\text{C}_6\text{H}_5\text{N(R)Na}^k$	(62) ^j	168
$\text{NC(CH}_2\text{)}_{11}\text{CN}$	Cyclononadecanone ^a	$\text{C}_6\text{H}_5\text{N(R)Na}^k$	(73) ^j	168
$\text{NC(CH}_2\text{)}_{12}\text{CN}$	Cycloeicosane-1,11-dione ^{a,q,r}	$\text{C}_6\text{H}_5\text{N(R)Na}^k$	(70) ^j	168
$\text{NC(CH}_2\text{)}_{13}\text{CN}$	Cycloeicosanone ^a	$\text{C}_6\text{H}_5\text{N(R)Na}^k$	(79-85) ^j	169, 168
$\text{NC(CH}_2\text{)}_{14}\text{CN}$	Cycloheicosanone ^a	$\text{C}_6\text{H}_5\text{N(R)Na}^k$	(70) ^j	169
$\text{NC(CH}_2\text{)}_{15}\text{CN}$	Cyclodocosane-1,12-dione ^{a,r}	$\text{C}_6\text{H}_5\text{N(R)Na}^k$	(60) ^j	168
$\text{NC(CH}_2\text{)}_{16}\text{CN}$	Cyclodocosanone ^a	$\text{C}_6\text{H}_5\text{N(R)Na}^k$	(83) ^j	169

Note: References 231 to 583 are on pp. 197-203.

^a The intermediate was hydrolyzed and decarboxylated.

^j The cyclization was carried out under high-dilution conditions.

^k The aniline base was described only as a sodium alkyl aniline. A later reference (171) suggests that R is methyl.

^t Partial hydrolysis occurred during the isolation of this product.

^m The cyclization was carried out in concentrated solution.

^p The cyclic product from condensation of two moles of nitrile was also formed; see below.

^q This product was isolated partly as ketone and partly as iminonitrile.

^r The cyclic product from condensation of one mole of nitrile was also formed; see above.

THE DIECKMANN CONDENSATION

193


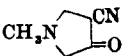
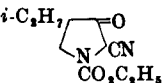
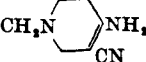
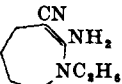
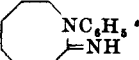
TABLE VI—Continued
THORPE-ZIEGLER CONDENSATIONS

194

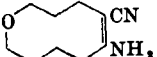
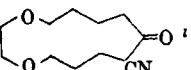
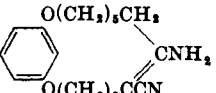
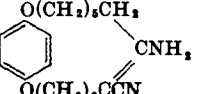
ORGANIC REACTIONS

E. Reactions Leading to Ten-Membered and Larger Rings				
Starting Nitrile	Product(s)	Base	Yield (%)	References
NC(CH ₂) ₁₀ CN	Cyclotricosanone ^a	C ₆ H ₅ N(R)Na ^b	(65) ^j	169
NC(CH ₂) ₁₁ CN	Cyclotetracosane-1,13-dione ^{a,r}	C ₆ H ₅ N(R)Na ^b	(—) ^j	168
NC(CH ₂) ₁₂ CN	Cyclotetracosanone ^a	C ₆ H ₅ N(R)Na ^b	(74) ^j	169
NC(CH ₂) ₁₃ CN	Cyclopentacosanone ^a	C ₆ H ₅ N(R)Na ^b	(64) ^j	169
NC(CH ₂) ₁₄ CN	Cyclohexacosane-1,14-dione ^{a,r}	C ₆ H ₅ N(R)Na ^b	(—) ^j	168
NC(CH ₂) ₁₅ CN	Cyclohexacosanone ^a	C ₆ H ₅ N(R)Na ^b	(68) ^j	169
NC(CH ₂) ₁₆ CN	Cyclooctacosanone ^a	C ₆ H ₅ N(R)Na ^b	(87) ^j	169
NC(CH ₂) ₁₇ CN	Cyclononacosanone ^a	C ₆ H ₅ N(R)Na ^b	(76) ^j	169
NC(CH ₂) ₁₈ CN	Cyclotriacontane-1,16-dione ^{a,r}	C ₆ H ₅ N(R)Na ^b	(18) ^j	165
NC(CH ₂) ₁₉ CN	Cyclotritriacontanone ^a	C ₆ H ₅ N(R)Na ^b	(68) ^j	169
NC(CH ₂) ₂₀ CN	Cyclotetratriacontane-1,17-dione ^{a,r}	C ₆ H ₅ N(R)Na ^b	(17) ^j	165

F. Reactions Leading to Heterocycles Containing Nitrogen

$\begin{array}{c} \text{CH}_2\text{CO}_2\text{C}_2\text{H}_5 \\ \\ \text{HN} \\ \\ \text{CH}_2\text{CH}_2\text{CN} \end{array}$		NaOC ₂ H ₅	(15)	559
$\begin{array}{c} \text{CH}_2\text{CH}_2\text{CN} \\ \\ \text{N}(\text{CH}_2\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5)_2 \end{array}$		NaOC ₂ H ₅	(—)	411
$\begin{array}{c} \text{N}(\text{CO}_2\text{C}_2\text{H}_5)_2\text{CH}_2\text{CN} \\ \\ \text{CH}_2\text{CH}(\text{C}_2\text{H}_5)_2\text{CO}_2\text{C}_2\text{H}_5 \end{array}$		Na	(60)	215
$\begin{array}{c} \text{CH}_2\text{N}(\text{CH}_2\text{CH}_2\text{CN})_2 \end{array}$		Na	(—)	411
$\begin{array}{c} \text{CH}_2\text{CH}_2\text{N}(\text{C}_2\text{H}_5)_2\text{CN} \\ \\ \text{CH}_2\text{CH}_2\text{CH}_2\text{CN} \end{array}$		C ₆ H ₅ N(CH ₃)Li	(93) ^j	402
$\begin{array}{c} \text{CH}_2\text{CH}_2\text{N}(\text{C}_2\text{H}_5)_2\text{CN} \\ \\ \text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CN} \end{array}$		C ₆ H ₅ N(CH ₃)Na	(73) ^j	401

G. Reactions Leading to Heterocycles Containing Oxygen

$\begin{array}{c} \text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CN} \\ \\ \text{O} \\ \\ \text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CN} \end{array}$		C ₆ H ₅ N(CH ₃)Na	(5) ^j	170
$\begin{array}{c} \text{O}(\text{CH}_2)_4\text{CN} \\ \\ \text{CH}_2\text{CH}_2\text{O}(\text{CH}_2)_4\text{CN} \end{array}$		C ₆ H ₅ N(CH ₃)Na	(71) ^j	170
$\begin{array}{c} \text{O}(\text{CH}_2)_4\text{CN} \\ \\ \text{C}_6\text{H}_5 \\ \\ \text{O}(\text{CH}_2)_4\text{CN} \end{array}$		C ₆ H ₅ N(R)Na ^b	(54) ^j	166
$\begin{array}{c} \text{O}(\text{CH}_2)_4\text{CN} \\ \\ \text{C}_6\text{H}_5 \\ \\ \text{O}(\text{CH}_2)_4\text{CN} \end{array}$		C ₆ H ₅ N(R)Na ^b	(52) ^j	166

Note: References 231 to 583 are on pp. 197–203.

^a The intermediate was hydrolyzed and decarboxylated.

^j The cyclization was carried out under high-dilution conditions.

^b The aniline base was described only as a sodium alkyl aniline. A later reference (171) suggests that R is methyl.

ⁱ Partial hydrolysis occurred during the isolation of the product.

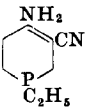
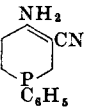
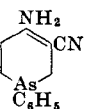
^r The cyclic product from condensation of one mole of nitrile was also formed; see above.

^s The product obtained had lost the nitrile group.

THE DIECKMANN CONDENSATION

195

TABLE VI—Continued
THORPE-ZIEGLER CONDENSATIONS

<i>H. Reactions Leading to Heterocycles Containing Phosphorus or Arsenic</i>				
Starting Nitrile	Product(s)	Base	Yield (%)	References
$\text{C}_2\text{H}_5\text{P}(\text{CH}_2\text{CH}_2\text{CN})_2$		$\text{KOC}_4\text{H}_9\text{-}t$	(83)	172
$\text{C}_6\text{H}_5\text{P}(\text{CH}_2\text{CH}_2\text{CN})_2$		$\text{KOC}_4\text{H}_9\text{-}t$	(80)	172
$\text{C}_6\text{H}_5\text{As}(\text{CH}_2\text{CH}_2\text{CN})_2$		$\text{KOC}_4\text{H}_9\text{-}t$	(—)	172

Note: References 231 to 583 are on pp. 197–203.

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CHAPTER 2

THE KNOEVENAGEL CONDENSATION

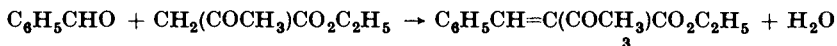
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CONTENTS

	PAGE
INTRODUCTION	205
MECHANISM	206
Evidence for the Knoevenagel Mechanism	208
Evidence for the Hann and Lapworth Mechanism	213
Decarboxylation during Malonic Acid Condensations	218
Formation of <i>bis</i> -(Active Methylene) Adducts	219
Stereochemical Aspects of the Knoevenagel Condensation.	220
SCOPE AND LIMITATIONS	222
Nature of the Active Methylene Component	223
Condensations with Malonic Acid	224
Condensations with Malonic Esters	229
Condensations with Malonamides	231
Condensations with Malononitrile	232
Condensations with Cyanoacetic Acid	236
Condensations with Cyanoacetic Esters	238
Condensations with Cyanoacetamides	244
Condensations with Ketones	246
Condensations with β -Ketonic Esters	249
Condensations with Nitro Compounds	254
Condensations with Sulfonyl and Related Compounds	257
Miscellaneous Active Methylene Compounds	258
COMPARISON WITH OTHER METHODS.	261
SELECTION OF EXPERIMENTAL CONDITIONS	264
Catalysts Other than Amines or Their Salts	266
EXPERIMENTAL PROCEDURES	267
TABULAR SURVEY	273

primary and secondary amines. In all cases *bis* condensation products similar to **1** and **2** were formed. In 1896 Knoevenagel reported that benzaldehyde and ethyl acetoacetate condensed at room temperature in the presence of piperidine to give a *bis* compound, but that when the reaction was run in a freezing mixture the product was ethyl benzylidene-acetoacetate (**3**).⁵ Subsequent investigation of this simpler condensation showed its wide generality.



For the purposes of this review the Knoevenagel condensation is defined as the reaction between an aldehyde or ketone and any compound having an active methylene group, brought about by an organic base or ammonia or their salts. The activation of the methylene group is due to the direct attachment of a group such as nitro, cyano, or acyl, and in most cases two such groups are required to provide sufficient activation. The primary product is usually an unsaturated compound, but it may undergo a Michael addition reaction with a second molecule of the active methylene compound to give *bis* compounds of type **1**. Excluded from consideration are condensations catalyzed by strong bases such as sodium hydroxide or quaternary ammonium hydroxides.

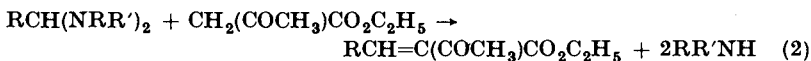
MECHANISM

Two principal mechanisms have been proposed for the Knoevenagel condensation. The first is based on Knoevenagel's mechanistic investigation, in which he attempted to obtain possible intermediates in the reaction and to cause these to react further.^{6, 7} Arylidene- or alkylidene-acetoacetates could be obtained:⁶

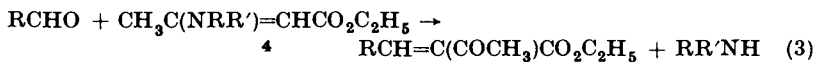
From the aldehyde, ethyl acetoacetate, and ammonia or an amine (primary or secondary),



From the alkylidene-*bis*-amines and ethyl acetoacetate,



From the aldehyde and a β -dialkylaminocrotonic ester,

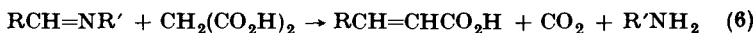
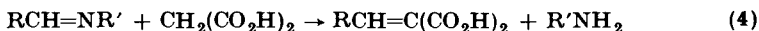


⁵ Knoevenagel, *Ber.*, **29**, 172 (1896).

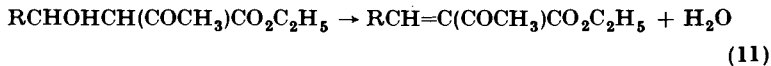
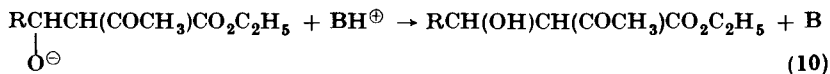
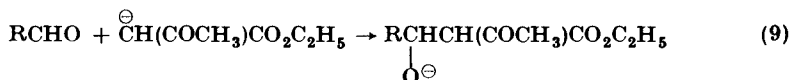
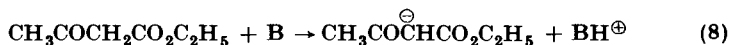
⁶ Knoevenagel, *Ber.*, **31**, 738 (1898).

⁷ Knoevenagel, *Ber.*, **31**, 2596 (1898).

Since some compounds that are reactive in the Knoevenagel condensation could not form intermediates of type 4, Knoevenagel assumed that the condensation proceeded by a route similar to (2), and that the role of the amine was to combine with the aldehyde forming a *bis*-(dialkylamino) compound or a Schiff base. The hypothesis was tested by studying the reactions of a wide range of such compounds with malonic acid as shown in equations 4-5 (at low temperature) and 6-7 (at high temperature).⁷



After it had been shown that pyridine was an effective catalyst in the Knoevenagel condensation,⁸⁻¹³ Hann and Lapworth proposed an alternative mechanism in which the function of the base was to remove a proton from the active methylene component forming a carbanion which then added to the aldehyde.¹⁴ Although Lapworth was subsequently



quoted as favoring an alternative mechanism which is akin to the Knoevenagel mechanism,¹⁵ the two mechanisms shown above are those which will be discussed in detail.

⁸ Verley, *Bull. Soc. Chim. France*, [3] **21**, 414 (1899).

⁹ Doebner, *Ber.*, **33**, 2141 (1900).

¹⁰ Doebner, *Ber.*, **34**, 54 (1901).

¹¹ Doebner, *Ber.*, **35**, 1137 (1902).

¹² Doebner, *Ber.*, **35**, 1147 (1902).

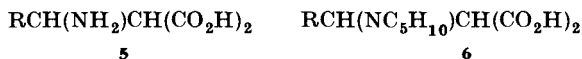
¹³ Doebner, *Ber.*, **35**, 2137 (1902).

¹⁴ Hann and Lapworth, *J. Chem. Soc.*, **85**, 46, (1904).

¹⁵ Hope and Robinson, *J. Chem. Soc.*, **99**, 2117 (1911).

Evidence for the Knoevenagel Mechanism

Evidence supporting the Knoevenagel mechanism (or simple variants thereon) has been provided mainly by the isolation of nitrogen-containing intermediates which could be further treated to give the normal condensation product. A study of the condensation of aromatic aldehydes with malonic acid using aniline as catalyst led to the observation that the benzalmalonic acid (equation 4) was not an intermediate in the formation of the cinnamic acid (equation 6), since benzalmalonic acid failed to decarboxylate under the conditions in which cinnamic acid was formed.¹⁶ It was concluded that the first intermediate was a Schiff base which combined with the malonic acid to give an intermediate aminodicarboxylic acid which in turn lost carbon dioxide and a molecule of amine to give the cinnamic acid. Support for this view seemed to be provided by reports of the isolation of amino malonic acids of types 5 and 6 when aldehydes were treated with malonic acids and alcoholic ammonia or an amine.¹⁷ These supposed amino acids were subsequently shown to be



ammonium or amine salts of the corresponding alkylidene- or arylidene-malonic acid, since they could be prepared from the malonic acid and ammonia or the appropriate amine and still contained a double bond (see equation 12).¹⁸



An intensive study of the system benzaldehyde-malonic acid-ammonia showed the immediate formation of benzhydramide, which could react further by slow hydrolysis to the aldehyde ammonia (the equivalent of the Schiff base in reactions with primary amine catalysts), and condensation of the aldehyde ammonia with malonic acid (reactions 13–15).¹⁹ The last step was shown to be quantitative in alcoholic solution. An alternative reaction path (equations 16 and 17), in which malonic acid added to the benzhydramide, led to the β -aminopropionic acids which had been isolated by Rodionov and his co-workers.²⁰

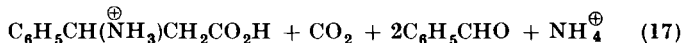
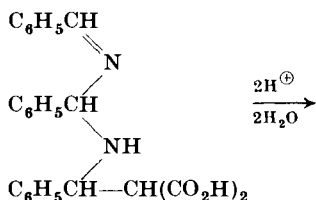
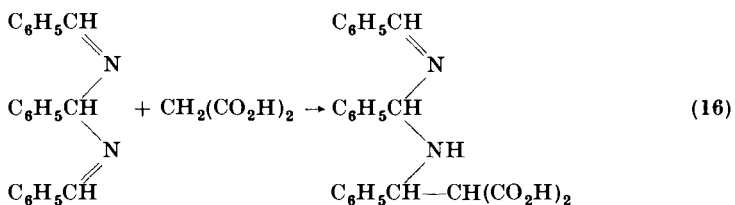
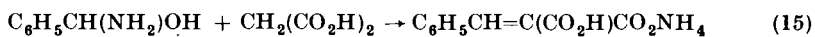
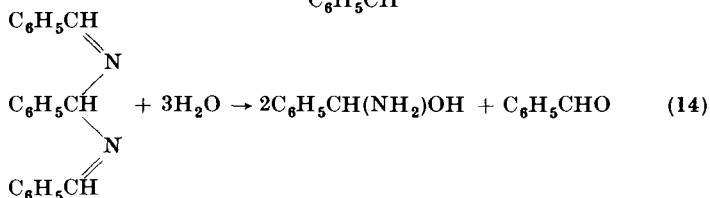
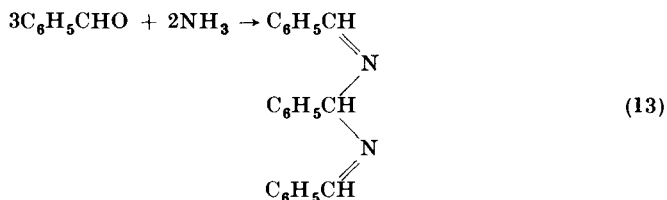
¹⁶ Rosenmund and Boehm, *Ann.*, **437**, 144 (1924).

¹⁷ Rodionov, *J. Am. Chem. Soc.*, **51**, 850 (1929).

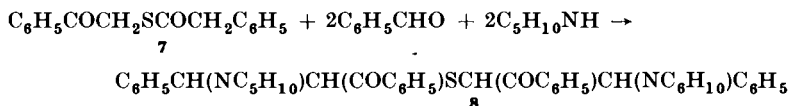
¹⁸ Boehm, *Arch. Pharm.*, **267**, 702 (1929).

¹⁹ Boehm and Grohnwald, *Arch. Pharm.*, **274**, 329 (1936).

²⁰ Rodionov and Malevinskaia, *Ber.*, **59**, 2952 (1926).



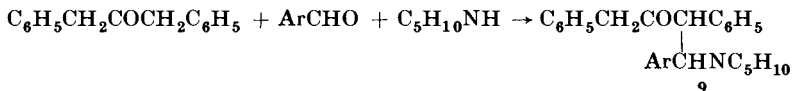
The most convincing evidence for a nitrogen-containing intermediate in the Knoevenagel condensation is provided by a series of papers by Dilthey and his associates. When compound 7 was condensed with benzaldehyde in the presence of piperidine, a condensation product was obtained, formulated as 8, in which two molecules of piperidine were covalently bound.²¹



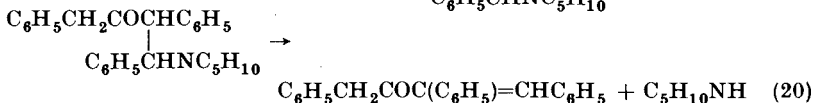
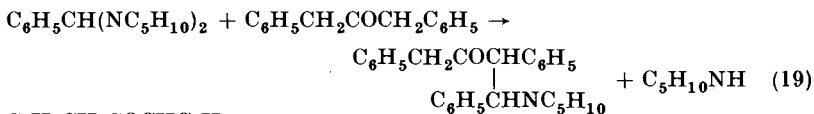
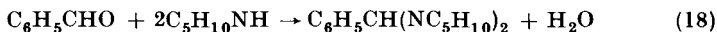
A more general study using dibenzyl ketone, which contains only one methylene group active in most condensation reactions, showed that

²¹ Dilthey and Lachs, *Ber.*, **60**, 1403 (1927).

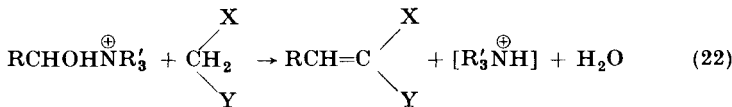
interaction with aromatic aldehydes and piperidine gave both racemates of type 9.²² Treatment of each racemate with acid leads to elimination



of a molecule of piperidine and formation of an arylidene dibenzyl ketone. The products of each stage of the reaction sequence 18–20 could be isolated, and the first two shown to react further to give the arylidene dibenzyl ketone.²³ The rate of the condensation was qualitatively correlated with



the stability of the *bis*-piperidide $\text{RCH}(\text{NC}_5\text{H}_{10})_2$. The *bis*-piperidide from *m*-nitrobenzaldehyde is very stable, and condensation of *m*-nitrobenzaldehyde with dibenzyl ketone and piperidine takes about 2 weeks, whereas with the very labile acetaldehyde *bis*-piperidide reaction is almost instantaneous. In condensations in which aniline or other primary amines were used, the active reagent was assumed to be the Schiff base, and it was shown that aniline does not add to the arylidene dibenzyl ketones under the conditions of the Knoevenagel condensation.²⁴ Hence the formation of compounds of type 9 occurs before the formation of the arylidene dibenzyl ketones. In reactions between aldehydes and ethyl acetoacetate, acetylacetone, or desoxybenzoin with a variety of basic catalysts, nitrogen-containing intermediates were isolated.²⁵ It was suggested that condensations involving tertiary amines proceeded through the amine salts, since the pure amines were not reactive (equations 21 and 22).



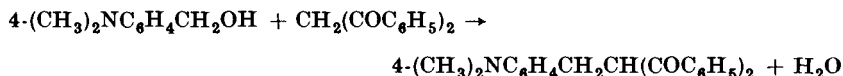
²² Dilthey and Stallman, *Ber.*, **62**, 1603 (1929).

²³ Dilthey, *Ber.*, **62**, 1609 (1929).

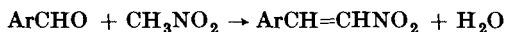
²⁴ Dilthey and Nagel, *J. Prakt. Chem.*, [2] **130**, 147 (1931).

²⁵ Dilthey and Steinborn, *J. Prakt. Chem.*, [2] **133**, 219 (1932).

p-Dimethylaminobenzyl alcohol has been used as a model for a proposed aldehyde ammonia intermediate and found to condense with dibenzoylmethane at high temperatures to give the expected condensation product.²⁶



The participation of Schiff base intermediates has been proposed for the condensation of aldehydes with nitromethane in the presence of ammonia or primary amines.²⁷ With primary amines the final product of the condensation is a nitroethylene or nitrostyrene **10**, and it has been suggested that the rate of reaction is dependent on the stability of the initially formed Schiff base. *o*-Chloro- and *m*-nitro-benzaldehyde both



10

condensed more rapidly than benzaldehyde with nitromethane in the presence of secondary or tertiary amines, but much more slowly than benzaldehyde when primary amines were used. Both have an aldehyde group which is more reactive than benzaldehyde in condensation reactions, but both also form a more stable Schiff base than benzaldehyde.

It has been claimed that the use of a Schiff base in place of an aldehyde leads to improved yields in the condensation with nitromethane and other nitro compounds.²⁸ The only kinetic studies supporting the Schiff base intermediate involve the condensation of aromatic aldehydes with nitromethane. In the condensation of 3-methoxy-4-hydroxybenzaldehyde with nitromethane in the presence of ammonium acetate, all experiments showed an induction period which could be eliminated by a preliminary mixing of the aldehyde and ammonium acetate.²⁹ It was suggested that the induction period represented the formation of an aldehyde imine as the first stage of the condensation. In accord with this suggestion, ammonium acetate and *n*-butylammonium acetate gave the fastest reaction, secondary and tertiary amine acetates being much less effective. In the reaction between 3,4-methylenedioxybenzaldehyde (piperonal) and nitromethane in the presence of *n*-butylamine, the rate of formation of the Schiff base and the rate of the reaction between the Schiff base and nitromethane were measured separately and the combined

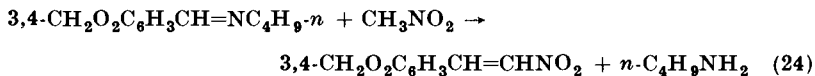
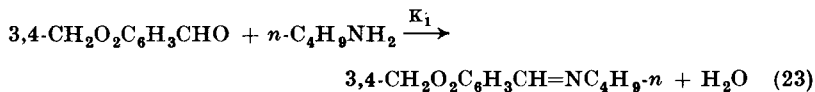
²⁶ Smith and Welch, *J. Chem. Soc.*, **1934**, 1136.

²⁷ Worrall, *J. Am. Chem. Soc.*, **56**, 1556 (1934).

²⁸ Robertson, *J. Org. Chem.*, **25**, 49 (1960).

²⁹ Crowell and Ramirez, *J. Am. Chem. Soc.*, **73**, 2268 (1951).

rates compared with that of direct combination between the aldehyde and nitromethane with *n*-butylamine added.³⁰

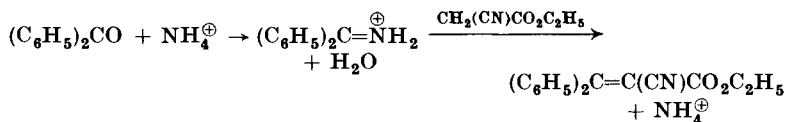


The conclusion was drawn that the overall rate approximated the one calculated from equations 23 and 24 separately, but the results are not entirely convincing because of difficulties in rate determination in reaction 24. Small amounts of added water were found to depress the rate of this condensation considerably, and the effect was ascribed to depression of Schiff base formation in reaction 23.³¹ By a spectrophotometric determination of Schiff base concentration in reaction 23 and determination from this of the rate

$$K_1 = \frac{[\text{ArCH=NC}_4\text{H}_9\text{-}n][\text{H}_2\text{O}]}{[n\text{-C}_4\text{H}_9\text{NH}_2][\text{ArCHO}]}$$

it was possible to calculate the proportion of Schiff base present in any mixture of aldehyde and *n*-butylamine. Using such calculated values in a plot of rate of condensation of piperonal and nitromethane over a range of concentrations a satisfactory straight line was obtained, indicating second-order kinetics (first order in Schiff base and first order in nitromethane). It was concluded that a Schiff base intermediate (or its conjugate acid) satisfactorily explained the kinetic results obtained.

The most recent and extensive investigation of the possible intermediate formation of Schiff bases or imines is due to Charles.³² By using imines or *N*-substituted imines a number of condensations were achieved with active methylene compounds and a general mechanism proposed. It was also suggested that the condensation of benzophenone with ethyl cyanoacetate using ammonium acetate as catalyst proceeded via an imine or imonium intermediate. This reaction is further discussed in the following section (p. 245).



³⁰ Crowell and Peck, *J. Am. Chem. Soc.*, **75**, 1075 (1953).

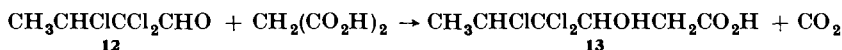
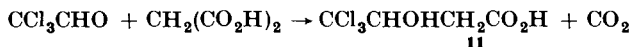
³¹ Bell and Crowell, *J. Org. Chem.*, **24**, 1159 (1959).

³² Charles, *Bull. Soc. Chim. France*, **1963**, 1559, 1566, 1573, 1576.

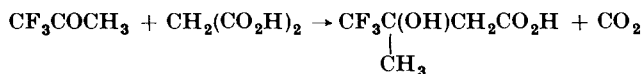
Evidence for the Hann and Lapworth Mechanism

The essential points of the second reaction mechanism are that the base removes a proton from the methylene component and that the resonance-stabilized anion adds to the carbonyl component, giving an intermediate hydroxyl compound. The evidence for this mechanism rests partly on isolation of hydroxyl-containing intermediates and partly on kinetic studies.

An early example of an intermediate of the aldol type is the β -hydroxy acid **11**, isolated from the reaction of chloral with malonic acid. The trichloroaldehyde **12** gave the acid **13**.³³ Additional examples are

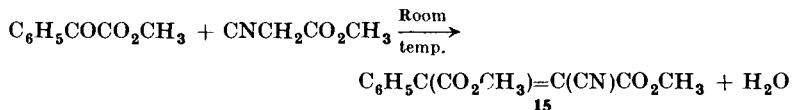
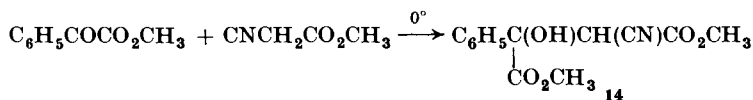


provided by the reaction of trifluoroacetone³⁴ and perfluoro-di-*n*-propyl ketone³⁵ with malonic acid. Other fluoro and chloro compounds react



similarly.³⁶

Condensation of methyl benzoylformate with methyl cyanoacetate using a mixture of methylamine hydrochloride and sodium carbonate at 0° gave the hydroxyl compound **14**; at room temperature the product was the unsaturated compound **15**.³⁷ Most of the other intermediates of the



aldol type that have been isolated require much more drastic conditions for dehydration. The reactions of methyl benzoylformate constitute examples of a non-enolizable ketone condensed successfully under

³³ Riedel and Straube, *Ann.*, **367**, 40 (1909).

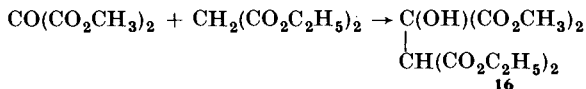
³⁴ Walborsky, Baum, and Loncrini, *J. Am. Chem. Soc.*, **77**, 3639 (1955).

³⁵ McBee, Kim, and Braendlin, *J. Am. Chem. Soc.*, **84**, 3155 (1962).

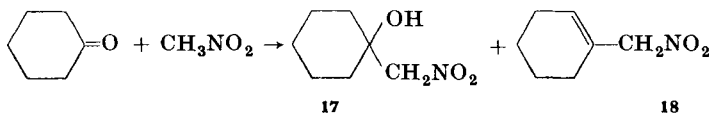
³⁶ McBee, Roberts, and Wilson, *J. Am. Chem. Soc.*, **79**, 2324 (1957).

³⁷ Kohler and Corson, *J. Am. Chem. Soc.*, **45**, 1975 (1923).

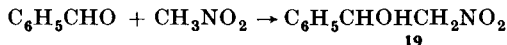
Knoevenagel conditions, contrary to a suggestion that enolization is a necessary first step.³⁸ A similar example is the condensation of dimethyl mesoxalate with diethyl malonate to give the hydroxy ester **16**.³⁹



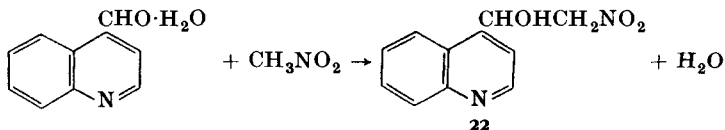
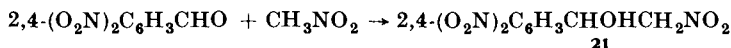
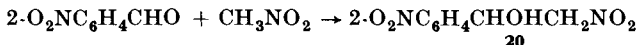
Condensations involving nitro compounds provide a number of examples in which either a hydroxy nitro compound or an unsaturated nitro compound can be obtained, along with the *bis*-dinitro compound formed by Michael addition to the unsaturated nitro compound. Cyclohexanone and nitromethane in the presence of piperidine at room temperature give a mixture of the hydroxyl compound **17** and the unsaturated compound formulated as **18**.⁴⁰



When secondary or tertiary amines were used, benzaldehyde condensed with nitromethane to give the hydroxyl compound **19**.²⁷ It was suggested that the catalysts were the protonated secondary or tertiary amines, but that primary amine catalysis involved formation of a Schiff base.²⁷ (See p. 211). Other examples of hydroxy nitro intermediates are provided by



the condensations of 2-nitrobenzaldehyde,⁴¹ 2,4-dinitrobenzaldehyde,⁴¹ and cinchoninic aldehyde hydrate⁴² with nitromethane to give compounds **20**, **21** and **22**, respectively.



Stabilization of the hydroxyl compounds **20** and **21** is attributed to the electron-withdrawing nitrophenyl groups. A similar explanation could

³⁸ Harding, Haworth, and Perkin, *J. Chem. Soc.*, **93**, 1943 (1908).

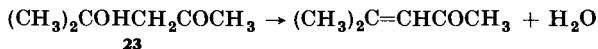
³⁹ Corson, Hazen, and Thomas, *J. Am. Chem. Soc.*, **50**, 913 (1928).

⁴⁰ Fraser and Kon, *J. Chem. Soc.*, **1934**, 606.

⁴¹ Fieser and Daudt, *J. Am. Chem. Soc.*, **68**, 2248 (1946).

⁴² Phillips, *J. Am. Chem. Soc.*, **70**, 453 (1948).

be applied to compound **22** and to the chloro and fluoro compounds previously mentioned. A study of the dehydration of aldols such as **23**, similar to those postulated as intermediates in the Knoevenagel condensation, has shown that many salts of piperidine and the hydrochlorides of a number of other amines can act as catalysts in the dehydration, whereas quaternary ammonium salts do not.⁴³



The suggestion that amine salts or the protonated amines were the active catalysts in the Knoevenagel condensation has been advanced by a number of authors.^{27, 44, 45} In particular, it was pointed out that pure aldehydes were rarely used and hence usually contained appreciable quantities of acid, while in other reactions the methylene component was itself an acid.⁴⁵ Similarly, when pure aldehydes were used, the reaction was rarely run in the absence of light and air. The discovery that ammonium acetate and amine acetates were effective catalysts for the Knoevenagel condensation⁴⁶ added weight to this suggestion, and data obtained by Cope and his co-workers supported an aldol-like mechanism.⁴⁷ Thus in the Hann and Lapworth scheme, equations 25–27, the salt (e.g., piperidinium acetate) could function as a base for the first stage (25) and as an acid for the third stage (27). The rate of the second stage (26), as with other carbonyl addition reactions, would depend on the relative bulk of the alkyl substituents attached to the carbonyl group.



A number of investigations have been made of the Knoevenagel condensation in aqueous alcoholic solution. The reaction between furfural and malonic acid in water using glycine as catalyst gave furfural-malonic acid.⁴⁸ Reinvestigation of this reaction showed that no condensation occurred in the absence of glycine.⁴⁹ Using a more reactive

⁴³ Canonica, Cardani, and Trave, *Atti. Acad. Nazl. Lincei, Rend. Classe Sci. Fis. Mat. Nat.*, **14**, 814 (1953) [*C.A.*, **49**, 4523 (1955)].

⁴⁴ Blanchard, Klein, and MacDonald, *J. Am. Chem. Soc.*, **53**, 2809 (1931).

⁴⁵ Kuhn, Badstübner, and Grundmann, *Ber.*, **69**, 98 (1936).

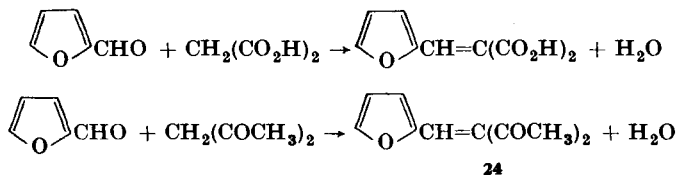
⁴⁶ Cope, *J. Am. Chem. Soc.*, **59**, 2327 (1937).

⁴⁷ Cope, Hofmann, Wyckoff, and Hardenbergh, *J. Am. Chem. Soc.*, **63**, 3452 (1941).

⁴⁸ Dakin, *J. Biol. Chem.*, **7**, 49 (1909).

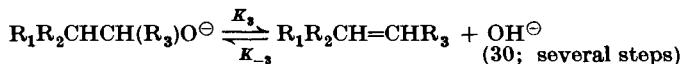
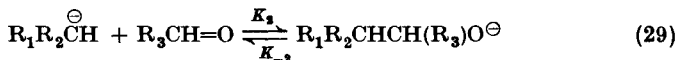
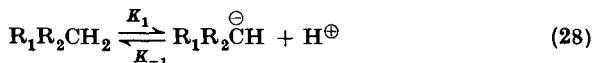
⁴⁹ Haley and Maitland, *J. Chem. Soc.*, **1951**, 3155.

methylene component (acetylacetone) it was found that condensation occurred with furfural in aqueous medium without glycine if the solution was buffered in the *pH* range 3–6.5. The product was not pure. With



glycine as catalyst (giving a solution in the *pH* range 4.1–4.4) yields of up to 92% of pure product **24** could be achieved, the yield varying with the concentration of glycine (though the highest yields may have been due partly to a salting-out effect at the high glycine concentrations). The suggestion was made that the first stage was protonation of the aldehyde, followed by a modification of the Hann and Lapworth mechanism.

The most extensive kinetic studies on the Knoevenagel condensation have been those of Patai and his associates.^{50–54} A spectrophotometric method was used to follow the course of the condensation, and aqueous or alcoholic solutions were used. In condensations between aromatic aldehydes and malononitrile, cyanoacetamide, or cyanoacetic ester, no catalyst was required, but, with diethyl malonate, piperidinium acetate was used. In all cases added acid decreased the rate of condensation appreciably, and in sufficient concentration stopped the reaction completely. Added salts such as lithium nitrate and lithium chloride increased the rate, though to a more limited extent. This was taken as evidence that the first stage in all condensations was ionization of the active methylene component, prevented by added acid (in the first step of the generalized Hann and Lapworth scheme shown in equations 28–30).



⁵⁰ Patai, Israeli, and Zabicky, *Chem. & Ind. (London)*, **1957**, 1671.

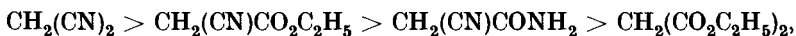
⁵¹ Patai and Israeli, *J. Chem. Soc.*, **1960**, 2020.

⁵² Patai and Israeli, *J. Chem. Soc.*, **1960**, 2025.

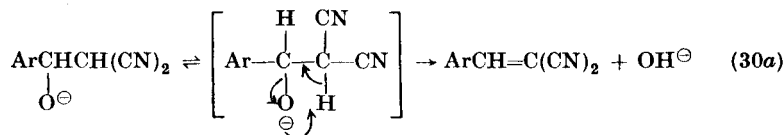
⁵³ Patai and Zabicky, *J. Chem. Soc.*, **1960**, 2030.

⁵⁴ Patai, Israeli, and Zabicky, *J. Chem. Soc.*, **1960**, 2038.

The rate of the reverse reaction was also depressed by added acid. It should be noted, however, that the reaction was first-order only with malononitrile in aqueous solution. In alcoholic solution, condensations with malononitrile showed second-order kinetics which were ascribed to very rapid ionization (K_1) following by a slower, rate-determining reaction (K_2). In accord with this interpretation, the rates for condensation of aromatic aldehydes with malononitrile in alcohol varied with the nature of the substituent in the para position in the order *p*-nitrobenzaldehyde > benzaldehyde > 4-methoxybenzaldehyde. Piperidine had a strong catalytic effect, but addition of benzoic acid to the piperidine-catalyzed mixtures depressed the rate. Condensations with cyanoacetamide showed kinetics between first and second order, approaching second order with an unreactive aldehyde such as 4-methoxybenzaldehyde ($K_1 > K_2$), but being closer to first order with more reactive aldehydes ($K_2 > K_1$). The order of reactivity for active methylene components was determined as

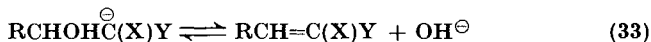


although the position of ethyl cyanoacetate is out of line with its dissociation constant. In condensations using malononitrile the same rate was observed whether it was measured by disappearance of the aldehyde or by formation of the arylidene compound, and hence it appears that there is no accumulation of an aldol intermediate. A four-center transition state was suggested for the dehydration as shown in equation 30a. The



addition of acid hinders the reverse reaction by depressing the hydroxyl ion concentration.

A qualitative study of the geometry of the ethylenes formed in a number of Knoevenagel condensations has suggested the mechanism, shown in equations 31-33,^{55, 56} for the elimination step (30).



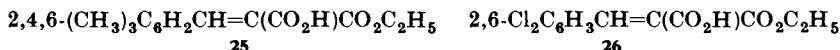
⁵⁵ Zabicky, *J. Chem. Soc.*, **1961**, 683.

⁵⁶ Zabicky, *J. Chem. Soc.*, **1961**, 687.

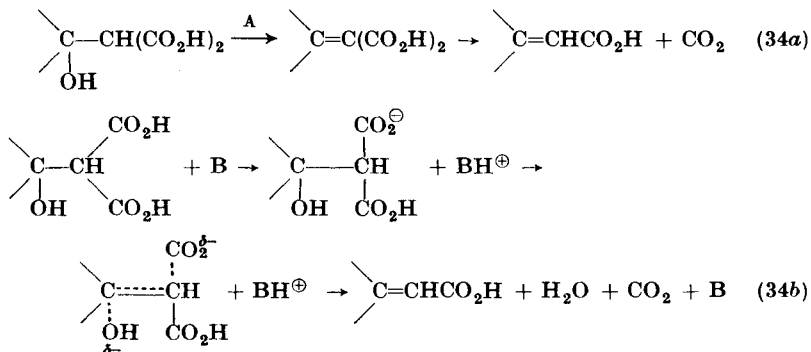
The most obvious general conclusion from the preceding discussion is that a single mechanism is unlikely for the wide range of Knoevenagel condensations. Even within the examples using a single type of active methylene component (such as the aliphatic nitro compounds) there is evidence for two mechanisms depending on the type of amine used (see p. 214). Condensations in polar media appear on the whole to favor the Hann and Lapworth mechanism, while the use of primary amines or ammonia favors the intermediate formation of imines or substituted imines.

Decarboxylation during Malonic Acid Condensations

Another aspect of the mechanism of the Knoevenagel condensation (or of the Verley-Doebner modification thereof^{8,9}) that has led to discussion is the accompanying decarboxylation in the condensation of aldehydes with malonic acid in pyridine at 100°. Corey found that the decarboxylation of ethyl hydrogen mesitylidenemalonate (**25**) and ethyl hydrogen 2,6-dichlorobenzylidene malonate (**26**) was slow in hot pyridine,⁵⁷ although the corresponding aldehydes condense readily with malonic acid under these conditions to give cinnamic acids. He concluded that ready



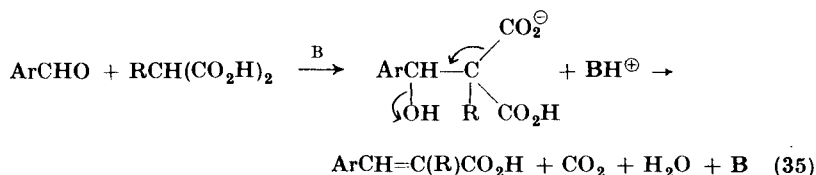
decarboxylation occurs only when a pathway is available that involves an α -carbon atom which does not carry a double bond. Hence, of the two pathways shown, **34a** is unlikely, and, in compounds in which an α -hydrogen atom is available, should lead to a mixture of α,β - and β,γ -unsaturated acids. Condensations in pyridine have been shown to give almost exclusively the α,β -unsaturated acid.⁵⁸



⁵⁷ Corey, *J. Am. Chem. Soc.*, **74**, 5897 (1952).

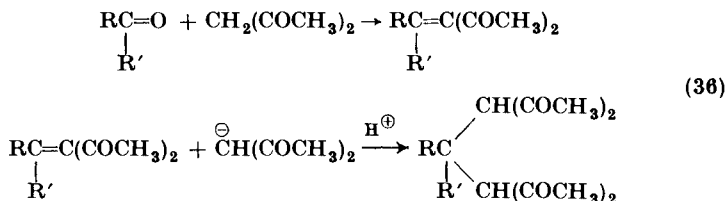
⁵⁸ Boxer and Linstead, *J. Chem. Soc.*, **1931**, 740.

Dehydration should be favored by solvents of high dielectric constant, whereas decarboxylative elimination should not. In triethanolamine as the solvent for condensations with malonic acid, a high proportion of β,γ -unsaturated acid is formed.⁵⁸ A study of the kinetics of the condensation between benzaldehyde and malonic acid in pyridine showed that most of the elimination of water preceded the decarboxylation and that the decarboxylation was first-order, conforming in rate with that of benzalmalonic acid in pyridine.⁵⁹ An elimination-decarboxylation reaction like that in equation 35 presumably operates in the condensation of aromatic aldehydes with alkylmalonic acids.⁶⁰



Formation of *bis*-(Active Methylene) Adducts

Many Knoevenagel condensation products are formed from one molecule of aldehyde or ketone and two molecules of active methylene component. With some active methylene compounds (notably β -ketoic esters and β -diketones) the *bis* adducts are obtained as frequently as the normal arylidene or alkylidene compounds. Since the evidence seems to favor Michael addition of a second molecule of methylene component to the initially formed unsaturated compound, as in (36), this reaction will not be discussed in detail here. A full discussion of the Michael addition reaction is available in *Organic Reactions*, Volume 10.



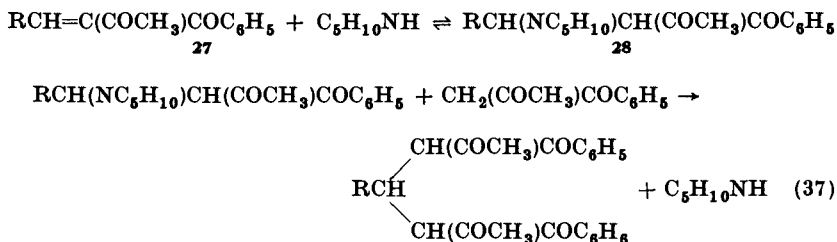
The alternative suggestion, that the second molecule of active methylene compound reacted directly with a nitrogen-containing intermediate formed by addition of a molecule of the amine to the unsaturated compound,⁶¹

⁵⁸ Patai, Edlitz-Pfeffermann, and Rozner, *J. Am. Chem. Soc.*, **76**, 3446 (1954).

⁵⁹ Genzler and Berman, *J. Am. Chem. Soc.*, **80**, 4949 (1958).

⁶¹ Ruhemann and Watson, *J. Chem. Soc.*, **85**, 1170 (1904).

was disproved by Dilthey and Steinborn.²⁵ They showed that the only conditions under which reaction 37 would occur were those in which the piperidine adduct **28** decomposed to give the unsaturated precursor **27**.

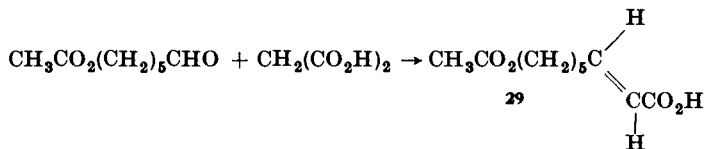


The unsaturated compound **27** added another molecule of active methylene compound on heating, even without a catalyst.

Stereochemical Aspects of the Knoevenagel Condensation

Steric effects on the course of the Knoevenagel condensation can be considered under two main headings. The first involves steric hindrance to the condensation, and examples are cited in the section, Scope and Limitations. The second concerns the stereochemical consequences of the reaction, especially as regards the geometrical isomers of the unsaturated products.

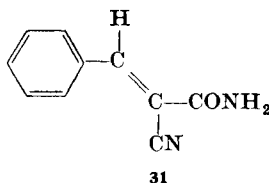
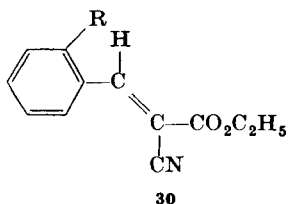
Condensations of malonic acid and aromatic aldehydes give rise to the *trans*-cinnamic acid exclusively in all products whose configurations have been determined. In the formation of this isomer, presumably, relief of steric strain in the intermediate malonic acid plays an important part. A number of condensations with aliphatic aldehydes also give rise to the *trans* product, e.g., the *trans*-acrylic acid. They have been used, for example, in the synthesis of the 8-acetoxyoctenoic acid **29**, and also of the ω -acetoxy-decenoic and -dodecenoic acids.⁶²



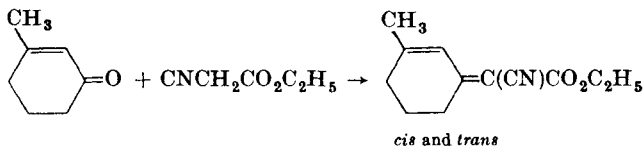
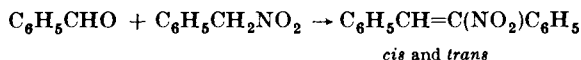
An extensive survey of condensation products from aromatic aldehydes and ethyl cyanoacetate or cyanoacetamide showed them to have the general configuration **30** (R = H) or **31** in which the *smaller* cyano group

⁶² Fray, Jaeger, Morgan, Robinson, and Sloan, *Tetrahedron*, **15**, 23 (1961).

was *cis* to the benzene ring.⁵⁵ In a specific spectrophotometric study 2-methoxybenzaldehyde was shown to give exclusively the *trans* product **30** ($R = OCH_3$), and there was no possibility that the *cis* form was first obtained with subsequent isomerization.⁶³



In contrast there are a number of reports of Knoevenagel condensations in which both *cis* and *trans* isomers are obtained. Examples are the condensation of benzaldehyde with phenylnitromethane⁶⁴ and of 1-methylcyclohexen-3-one with ethyl cyanoacetate.⁶⁵ A number of unsymmetrical diaryl and aralkyl ketones have been reported to condense with cyanoacetamide to give mixtures containing almost equal proportions of the two possible stereoisomers.⁶⁶



3,4,5-Trimethoxybenzaldehyde condenses with cyanoacetic acid in the presence of a solvent mixture of 7% piperidine and 93% pyridine to give both the *cis* and the *trans* cinnamic acid derivatives.⁶⁷ Of these, only the *cis* acid decarboxylates to give the cinnamitrile, **32**, while only the *trans* acid adds another molecule of cyanoacetic acid to give the glutaronitrile, **33**.

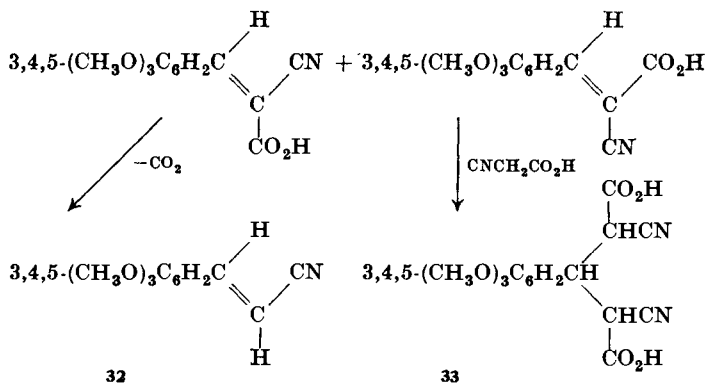
⁶³ Rappoport and Patai, *Bull. Res. Council Israel Sect. A*, **10A**, 149 (1961) [*C.A.*, **56**, 2341 (1962)].

⁶⁴ Heim, *Ber.*, **44**, 2016 (1911).

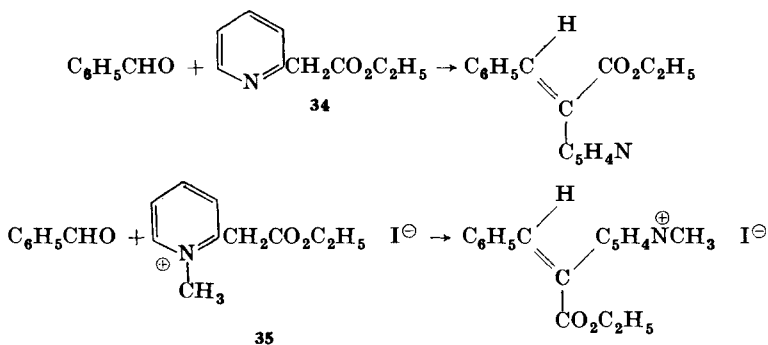
⁶⁵ Farmer and Ross, *J. Chem. Soc.*, **1928**, 1574.

⁶⁶ Foucaud, Person, and Robert, *Bull. Soc. Chim. France*, **1964**, 1873.

⁶⁷ Schiemenz and Engelhard, *Chem. Ber.*, **95**, 968 (1962).

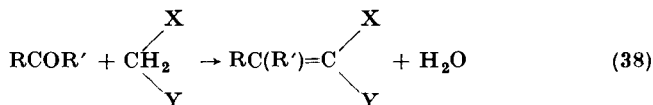


One notable difference in the steric course of reaction is furnished by the condensation of benzaldehyde with ethyl 2-pyridylacetate (**34**) and its methiodide (**35**). The former led to the *trans* ester, the latter to the *cis* ester.⁶⁸



SCOPE AND LIMITATIONS

In principle the Knoevenagel condensation is applicable to any aldehyde or ketone and any active methylene compound, although the conditions necessary may be drastic with some less reactive methylene groups. Steric effects may inhibit the reaction, and many condensations have led to unexpected products as a result of secondary reactions. The general equation shown below will be used to describe the scope of the condensation



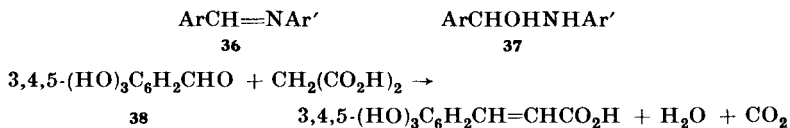
⁶⁸ Bragg and Wibberley, *J. Chem. Soc.*, **1961**, 5075.

Nature of the Active Methylene Component

The groups, represented by X and Y in the general equation, which have provided activation for the methylene group, are NO₂, quaternary pyridinium or similar heterocycles, CN, COR (and COAr), CONHR (and CONHAr), CO₂R, CO₂H, SO₂, S, Ar (particularly aryl groups carrying *ortho* or *para* electron-withdrawing substituents), pyridine and similar electron-deficient heterocycles. Two such groups are usually necessary for activation, but notable exceptions are the nitro group and quaternized pyridine or quinoline systems. Few attempts have been made to list the activating groups in order of effectiveness. One such study using benzaldehyde with various active methylene compounds gave a tentative order of decreasing effectiveness as NO₂ > COCH₃ > COC₆H₅ > C₆H₅, but it was emphasized that this order could be only approximate because of interaction between the groups X and Y by chelation, steric hindrance, and resonance.⁶⁹ Using compounds of the type RCH₂CO₂C₂H₅ it was shown that reactivity decreased in the order R = CN, COCH₃, and CO₂C₂H₅, and hence a more complete list reads NO₂ > CN > COCH₃ > COC₆H₅ > CO₂C₂H₅ > C₆H₅.

A number of investigations have led to the suggestion that variation in the aldehyde or ketone component leads to changes in both rate of reaction and yield. Ketones as a class are less reactive than aldehydes and, as a general rule, the members of each class which are least reactive in other carbonyl addition reactions are also least reactive in the Knoevenagel condensation. Examples of reduction in rate and yield due to steric hindrance will be mentioned later (pp. 228, 233, 238).

Investigations of the effect of substituents in aromatic aldehydes and ketones have led to conflicting results. With aniline as catalyst in the condensation of aromatic aldehydes with malonic acid, the rate of reaction was correlated with the tendency of the aldehyde to form a Schiff base 36 or a Schiff base hydrate 37.¹⁶ Most aldehydes form Schiff bases, but some hydroxy benzaldehydes form stable Schiff base hydrates and these fail to give the corresponding cinnamic acid. The trihydroxy benzaldehyde 38 can be converted to the cinnamic acid by the use of a stronger base (piperidine). Dilthey and Nagel's suggestion that the rate

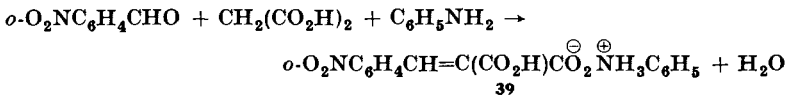


⁶⁹ Pratt and Werble, *J. Am. Chem. Soc.*, **72**, 4638 (1950).

of condensation depends on the stability of the Schiff base or the *bis*-(secondary amine) compound $\text{RCH}(\text{NR}'\text{R}'')_2$ has been mentioned before (p. 210).²⁴ These investigators found that *p*-nitrobenzaldehyde reacted more slowly than benzaldehyde, which in turn reacted more slowly than 4-methoxybenzaldehyde. This conclusion was confirmed by another group of chemists,⁶⁹ although a third group found a slight retardation in similar condensations with any *para* substituent.⁷⁰ On the other hand, in the condensation of malononitrile with aromatic aldehydes in 95% ethanol and with acetophenones in boiling benzene,⁷¹ an appreciable difference in reaction rate was observed. In the first case the fastest condensation was obtained with a *p*-nitro substituent, decreasing through *p*-chloro compounds to benzaldehyde itself, and thence to *p*-ethoxy and *p*-hydroxy substituents. In the acetophenones the fastest condensation was with a *p*-phenyl and a *p*-ethoxyl group, slower reaction with *p*-nitro, and much slower with a *p*-chloro group. An ebulliometric study of the condensation between aromatic aldehydes $\text{RC}_6\text{H}_4\text{CHO}$ and ethyl cyanoacetate in boiling 2% ethanolic triethylamine showed second-order kinetics, and the rates were reported to vary with change in substituent R in accord with the Hammett equation.⁷² No general order of reactivity can be laid down for the aldehyde or ketone component in the condensation.

Condensations with Malonic Acid (Tables I and III)

Reactions involving malonic acid as the active methylene compound make up the largest group. There are very few examples of condensation between ketones and malonic acid, but reactions involving every type of aldehyde are known. The most common products of this condensation are the alkylidene- or arylidene-malonic acids or the equivalent α,β -unsaturated monocarboxylic acids. To obtain the malonic acids the reagent of choice is alcoholic ammonia at a temperature below the boiling point of the reaction mixture; the ammonium salt has often been isolated.¹⁸ Using amines, but not piperidine, as catalysts, the isolation of the amine salt of the substituted malonic acid has been reported; thus *o*-nitrobenzaldehyde, malonic acid, and aniline at room temperature yield the salt 39.¹⁸

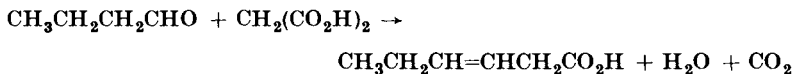


⁷⁰ Ogata and Tsuchida, *J. Am. Chem. Soc.*, **81**, 2092 (1959)

⁷¹ Mowry, *J. Am. Chem. Soc.*, **67**, 1050 (1945)

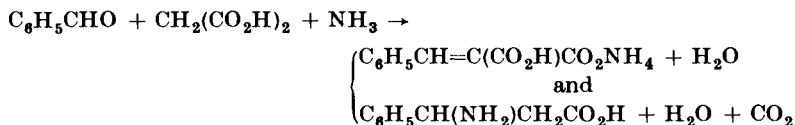
⁷² Heitler, *J. Chem. Soc.*, **1963**, 4885.

The preparation of acrylic or cinnamic acids is most frequently accomplished by heating the reactants in pyridine on a steam bath or under reflux until no more carbon dioxide is evolved. High temperatures are not essential, as the reaction proceeds even at room temperature.⁷³ One of the major advantages of malonic acid as an active methylene compound is that addition of a second molecule by a Michael reaction is very rare. Most of the examples known involve aliphatic aldehydes;^{58, 74} some 3-ethylglutaric acid is reported from the reaction between propionaldehyde and malonic acid using triethanolamine as catalyst, and the condensation of acetaldehyde with malonic acid in pyridine solution with some piperidine at 0° to -5° is reported to furnish 3-methylglutaric acid.⁵⁸ Catalysis by triethanolamine of the condensation of aliphatic aldehydes with malonic acid gives rise to high proportions of β,γ -unsaturated acids;⁵⁸ *n*-butyraldehyde gives 40–42% of 3-hexenoic acid. Most of the amines



that catalyze this condensation give appreciable quantities of β,γ -unsaturated acid; pyridine is unusual in producing high yields of α,β -unsaturated acid.⁵⁸

Among the secondary products that can be obtained in the Knoevenagel condensation using malonic acid are the β -amino acids isolated by Rodionov and his associates.²⁰ Initial reports that β -aminoalkylmalonic acids were obtained¹⁷ were not substantiated, and the supposed β -aminoalkylmalonic acids were shown to be the amine or ammonium salt of the malonic acid.¹⁸ At the same time it was shown that a substantial



yield of the β -amino monocarboxylic acid could be obtained, usually mixed with the corresponding cinnamic acid.

Hydroxy acid intermediates that are stabilized by negative substituents may be the main product of the reaction. If an appropriately placed carboxyl group is available as in **40** and **41**, a lactone may result.^{75–77}

⁷³ Zaar, *Ber. Schimmel & Co. A.-G.*, Jubilee Number, 299 (1929) [*C.A.*, **24**, 2107 (1930)].

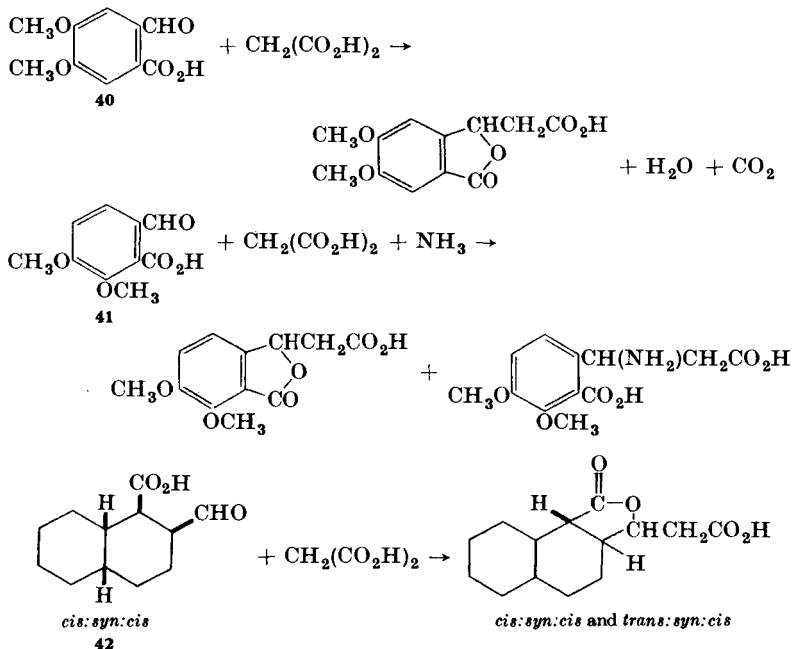
⁷⁴ Sircar, *J. Chem. Soc.*, **1928**, 55.

⁷⁵ Edwards, *J. Chem. Soc.*, **1928**, 748.

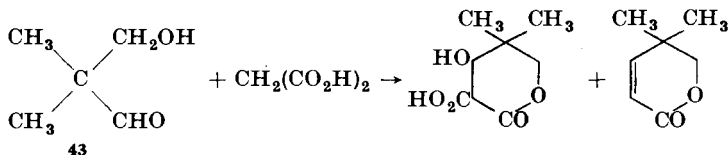
⁷⁶ Rodionov and Fedorova, *J. Am. Chem. Soc.*, **52**, 370 (1930).

⁷⁷ Rodionov and Kanevskaja, *Bull. Soc. Chim. France*, [5] **1**, 653 (1934).

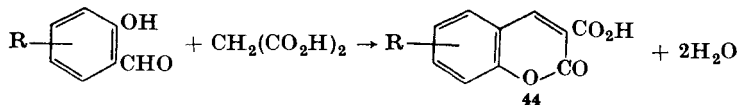
An alicyclic example is the conversion of the aldehyde **42** into the lactones shown.⁷⁸ A more usual lactonisation is that between a carboxylic acid



group in the product and an appropriately placed hydroxyl group. A simple example of this is furnished by the condensation of the aldol **43**, which forms both the hydroxy lactone and the unsaturated lactone.⁷⁹



Salicylaldehyde or substituted salicylaldehydes and malonic acid form coumarin-3-carboxylic acids such as **44** in good yield.^{7, 80}

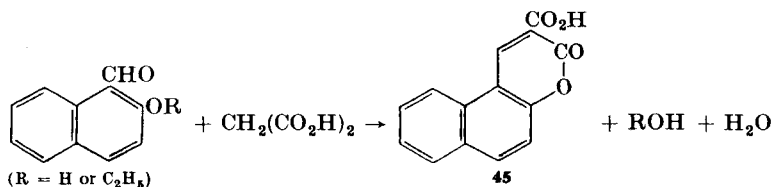


⁷⁸ Andreev, Kazaryan, and Kucherov, *Izv. Akad. Nauk SSSR, Ser. Khim.*, **1963**, 2003 [*C.A.*, **60**, 5356 (1964)].

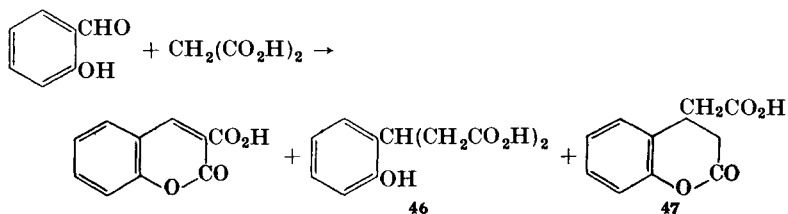
⁷⁹ Silberstein, *Monatsh. Chem.*, **25**, 13 (1904).

⁸⁰ Adams and Bockstahler, *J. Am. Chem. Soc.*, **74**, 5347 (1952).

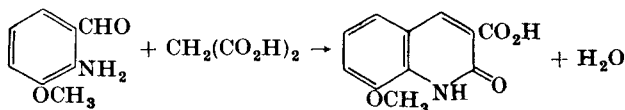
2-Hydroxy-1-naphthaldehyde⁸¹ and its ethyl ether⁸² yield the benzo-



coumarin 45. A few substituted salicylaldehydes are reported to give the arylidenemalonic acid;⁸³ and salicylaldehyde itself has been reported to give, in addition to coumarin-3-carboxylic acid, the substituted glutaric acid 46 and its lactone 47.⁸⁴



o-Aminobenzaldehydes and malonic acid yield carbostyryls.⁸⁵



The use of α -ketoaldehydes in the malonic acid condensation leads to the formation of aroylacrylic acids, but the yields are less than 50%.⁸⁶ Two modifications of the malonic acid condensation employ acetals in place of free aldehydes⁸⁷ and alkylmalonic acids in place of malonic acid.⁸⁸ In the first modification, from methyl hydrogen malonate and the acetal of cinnamaldehyde a high yield of the unsaturated malonic acid derivative 48 was obtained; the mechanism suggested for the reaction (which does not proceed through the free aldehyde) is shown in the reaction sequence 39. With malonic acid and various acetals the yield

⁸¹ Knoevenagel and Schröter, *Ber.*, **37**, 4484 (1904).

⁸² Sachs and Brigl, *Ber.*, **44**, 2098 (1911).

⁸³ Yasuda, *J. Sci. Res. Inst. (Tokyo)*, **52**, 95 (1958) [*C.A.*, **53**, 16052 (1959)].

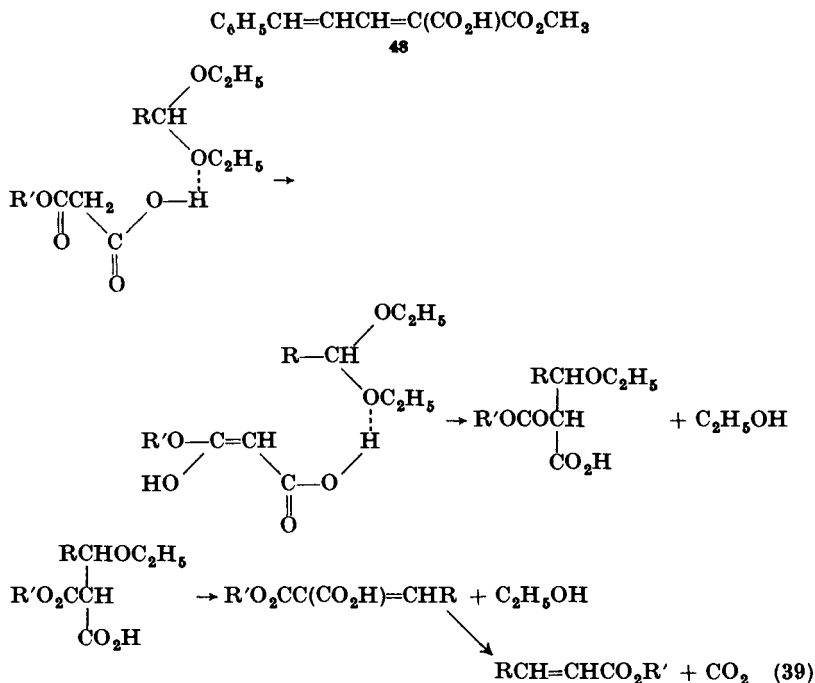
⁸⁴ Pandya and Pandya, *J. Indian Chem. Soc.*, **29**, 526 (1952).

⁸⁵ Tröger and St. Gero, *J. Prakt. Chem.*, [2] **113**, 293 (1926).

⁸⁶ Steinbach and Becker, *J. Am. Chem. Soc.*, **76**, 5809 (1954).

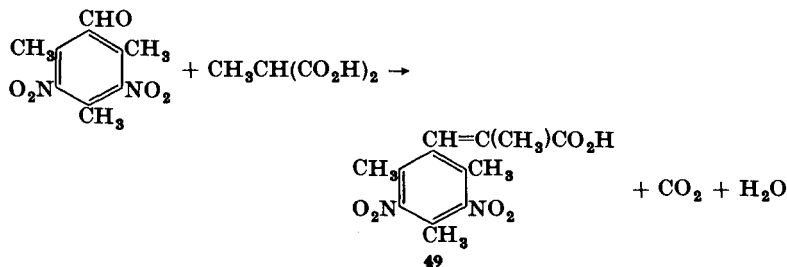
⁸⁷ Klein and Bergmann, *J. Am. Chem. Soc.*, **79**, 3452 (1957).

was poorer, but the recovery of unchanged acetal suggested that the rate was unfavorable.

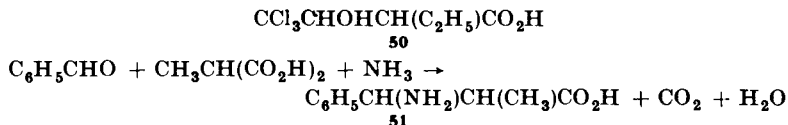


The condensation of an alkylmalonic acid with a wide range of aromatic aldehydes gives rise to the corresponding α -alkylcinnamic acid.⁶⁰ The condensation is more susceptible to steric hindrance than that with the unsubstituted malonic acid.

No condensation was achieved between substituted malonic acids and 2,4,6-trimethylbenzaldehyde, but the substituted cinnamic acid 49 was obtained in 14% yield from 3,5-dinitro-2,4,6-trimethylbenzaldehyde, indicating that steric hindrance is not the only factor involved. No condensations were achieved with isopropylmalonic acid.



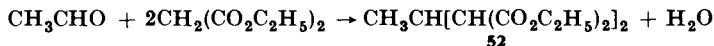
There are examples of the isolation of β -hydroxy acids, e.g., **50**, from alkylmalonic acids and aldehydes,⁸⁸ and of α -alkyl β -amino acids such as **51**, when alcoholic ammonia was used as the condensing agent.⁸⁹



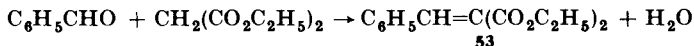
The unsaturated acids obtained in the Knoevenagel condensation are usually readily reduced to the corresponding saturated acids. By this method a great number of arylpropionic acids have been prepared. The cinnamic acids are usually readily decarboxylated to the corresponding styrenes, and the coumarincarboxylic acids to the corresponding coumarins. The double bond adds hydrogen halides and halogens, and the latter addition with subsequent dehydrohalogenation has been used to synthesize acetylenic acids. A more extensive discussion of synthetic uses of cinnamic acids is given in an earlier volume of *Organic Reactions*.⁹⁰

Condensations with Malonic Esters (Tables II and III)

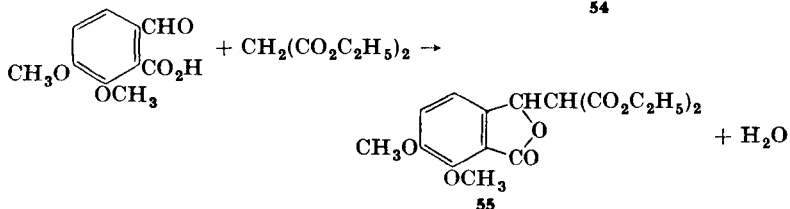
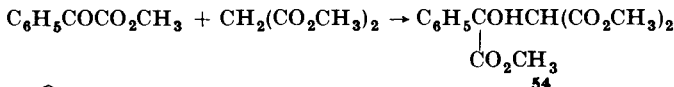
The majority of the condensations involving malonic esters have been performed with aldehydes. In the earliest examples excess malonic ester was used, leading to formation of alkylidene-*bis*-malonates such as **52**.² Subsequently it was discovered that most aldehydes will give



alkylidene- or arylidene-malonic esters such as **53**, the usual conditions of reaction being a secondary amine catalyst at water-bath temperature.



In a few cases β -hydroxy esters,³⁷ e.g., **54**, or lactones,⁷⁶ e.g., **55**, formed from these esters have been isolated.

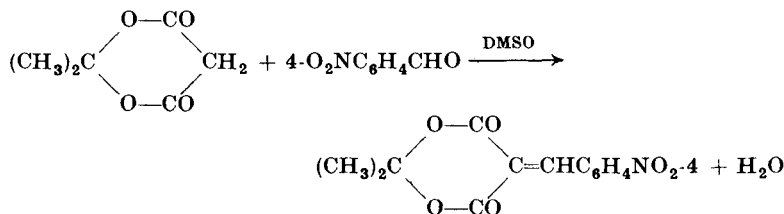


⁸⁸ Doebner and Segelitz, *Ber.*, **38**, 2733 (1905).

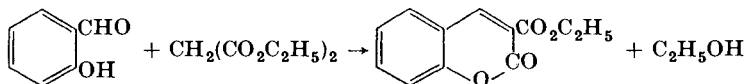
⁸⁹ Rodionov and Postovskaia, *J. Am. Chem. Soc.*, **51**, 841 (1929).

⁹⁰ Johnson, *Org. Reactions*, **1**, 240-252 (1942).

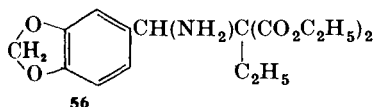
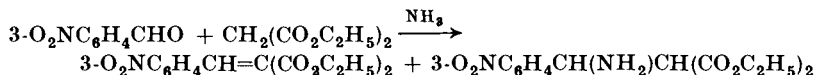
Isopropylidene and benzylidene malonates are very reactive in condensations with aldehydes, no catalysts being necessary if a very polar solvent (dimethylformamide or dimethyl-sulfoxide) is used.⁹¹



Condensation of malonic esters with salicylaldehydes gives esters of the corresponding coumarin-3-carboxylic acids.²

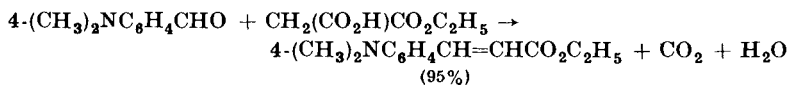


When ammonia or an amine in ethanol has been used as a catalyst, the arylidenemalonic ester obtained has occasionally been accompanied by smaller amounts of a β -aminoalkylmalonic ester.⁹² Alkylmalonic esters



have been used in this reaction to give β -aminoalkylmalonic esters such as **56**.⁸⁹

Partial hydrolysis of malonic acid diesters, using one mole of potassium hydroxide, furnishes alkyl hydrogen malonates in good yield.⁹³ The alkyl hydrogen malonates and aldehydes give cinnamic esters in excellent yield.⁹³



The alkylidene- and arylidene-malonic esters are readily reduced catalytically to give alkylmalonic esters. Metal hydrides, which have

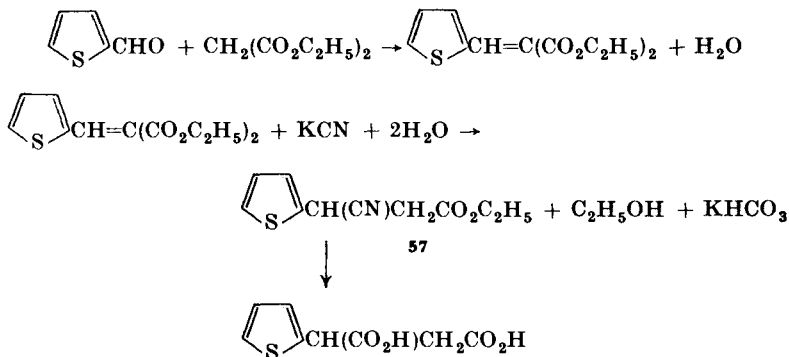
⁹¹ Hedge, Kruse, and Snyder, *J. Org. Chem.*, **26**, 3167 (1961).

⁹² Rodionov and Fedorova, *Ber.*, **60**, 804 (1927).

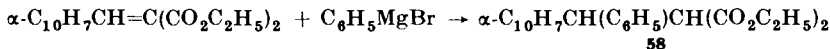
⁹³ Galat, *J. Am. Chem. Soc.*, **68**, 376 (1946).

been reported to reduce the double bond selectively in arylidenemalononitriles and arylidenecyanoacetic esters, were not satisfactory for this purpose with arylidenemalononic esters, the ester groups being reduced to give diols.⁹⁴ The double bond in the alkylidene- and arylidene-malonates is sufficiently active to undergo Michael addition reactions.⁹⁵

2-Thienylidenemalononic ester reacts with ethanolic potassium cyanide to give the cyanopropionic ester **57**, which can be hydrolyzed to the thienyl

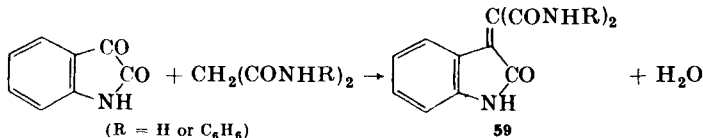


succinic acid in good yield.⁹⁶ Diethyl 1-naphthylidenemalonate reacts with phenylmagnesium bromide to give the ester **58**.⁹⁷



Condensations with Malonamides (Table IV)

Few condensations involving malonic acid diamide fall within the scope of this chapter. Isatin condenses with malonic acid amides to give compounds of type **59**.⁹⁸



The more complex reaction between 1,3-diketones and malonamide to give pyridones such as **60** may involve Michael additions rather than

⁹⁴ Le Moal, Carrie, and Bargain, *Compt. Rend.*, **251**, 2541 (1960).

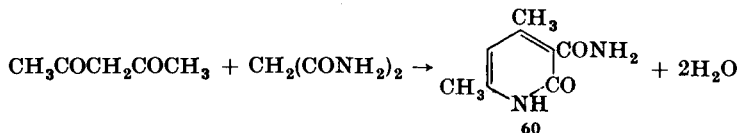
⁹⁵ Bergmann, Ginsburg, and Pappo, *Org. Reactions*, **10**, 179-555 (1959).

⁹⁶ Pettersson, *Arkiv. Kemi.*, **7**, 39 (1954).

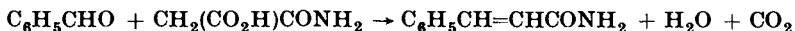
⁹⁷ Newman and Flanagan, *J. Org. Chem.*, **23**, 797 (1958).

⁹⁸ Lindwall and Hill, *J. Am. Chem. Soc.*, **57**, 736 (1935).

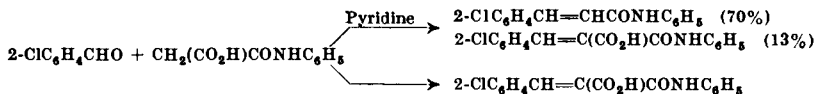
Knoevenagel condensations.⁹⁹ Many other examples are provided by the condensations involving malonamic acid and the malonic acid mono-anilides (malonanilic acids).



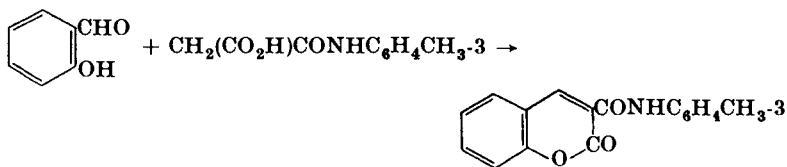
Malonamic acid, obtained by ammonolysis of methyl hydrogen malonate, condenses with aldehydes to give the corresponding acrylamide or cinnamamide; thus benzaldehyde gives cinnamamide.¹⁰⁰



A wide variety of malonanilic acids has been condensed with aromatic aldehydes, both with and without a basic catalyst (usually piperidine). The base-catalyzed condensations give primarily the cinnamanilide, while the uncatalyzed reactions give predominantly the arylidene-malonanilic acid.¹⁰¹ Salicylaldehyde reacts with malonanilic acids to



give anilides of coumarin-3-carboxylic acid.¹⁰²



Condensations with Malononitrile (Table V)

Malononitrile is one of the most reactive methylenic compounds in the Knoevenagel condensation. Many reactions proceed satisfactorily uncatalyzed, although the rates are increased by bases. Most of the products listed in Table V are formed by condensation between one

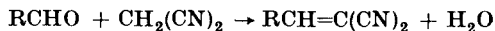
⁹⁹ Basu, *J. Indian Chem. Soc.*, **7**, 823 (1930).

¹⁰⁰ Galat, *J. Am. Chem. Soc.*, **70**, 2596 (1948).

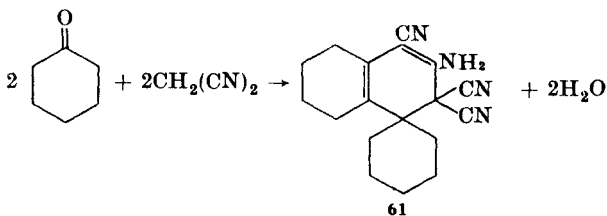
¹⁰¹ Pandya and Pandya, *Proc. Indian Acad. Sci.*, **17A**, 3 (1943) [*C.A.*, **37**, 4379 (1943)].

¹⁰² Ahluwalia, Haq, and Ray, *J. Chem. Soc.*, **1931**, 2059.

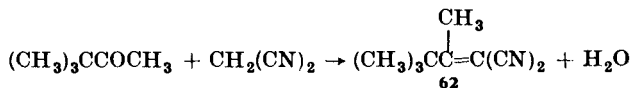
molecule of malononitrile and one molecule of carbonyl compound. Most condensations give a substituted 1,1-dicyanoethylene



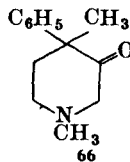
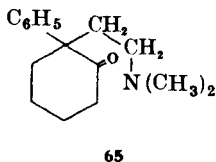
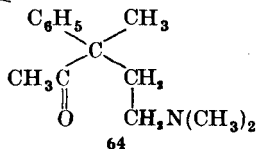
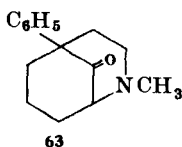
but cyclohexanone reacts with malononitrile to give a product **61**^{103, 104} (originally formulated as cyclohexylidenemalononitrile).¹⁰⁵



There are a number of examples of slow reaction or complete inactivity which have been attributed to steric hindrance in the carbonyl component. Pinacolone gives only 48% conversion to the dicyanoethylene **62** under conditions similar to those in which cyclohexanone and acetone gave over 90% condensation.¹⁰⁶ Of the related compounds **63–66**, the first has been



successfully condensed with malononitrile, while the last three failed to react.^{107, 108} It has been pointed out that the compounds which do not



condense are enolizable, while the one that does condense is not. Enolization of the bicyclo compound **63** would violate Bredt's rule.

¹⁰³ Weir and Hyne, *Can. J. Chem.*, **41**, 2905 (1963).

¹⁰⁴ Weir and Hyne, *Can. J. Chem.*, **42**, 1444 (1964).

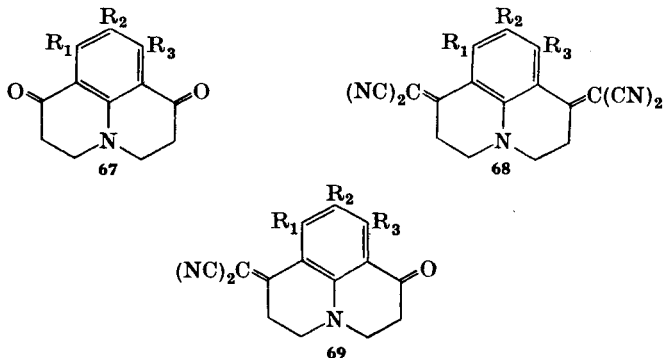
¹⁰⁵ Corson and Stoughton, *J. Am. Chem. Soc.*, **50**, 2828 (1928).

¹⁰⁶ Prout, *J. Org. Chem.*, **18**, 928 (1953).

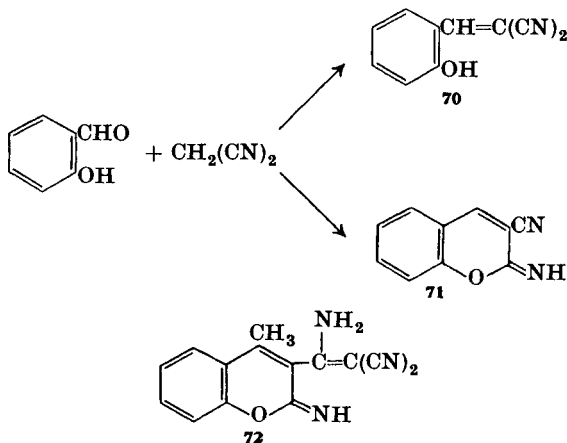
¹⁰⁷ May and Murphy, *J. Org. Chem.*, **19**, 620 (1954).

¹⁰⁸ May, *J. Org. Chem.*, **22**, 593 (1957).

A series of substituted julolidones shows very clear evidence of progressively increasing steric inhibition of the condensation with malononitrile.¹⁰⁹ The compounds **67** in which R_1 and $R_3 = H$ form *bis*-(dicyanomethylene) derivatives **68** regardless of whether R_2 is H, Cl, or C_6H_5 . Compounds in which R_3 is a methyl group form only a mono-(dicyanomethylene) derivative **69**, and compounds in which R_1 and R_3 are both methyl groups cannot be condensed at all with malononitrile.



Salicylaldehyde has been reported to condense with malononitrile to give the normal product, the dicyano styrene derivative **70**,¹¹⁰ but more recently the condensation has been shown to give also the coumarin imine **71**, which can be hydrolyzed to 3-cyanocoumarin.¹¹¹ A similar reaction has been reported between 2-hydroxyacetophenone and malononitrile, giving the more complex imine **72**.¹¹²



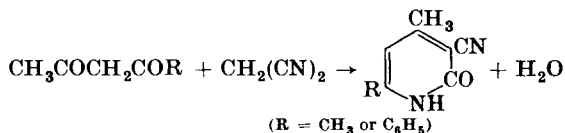
¹⁰⁹ Ittyerah and Mann, *J. Chem. Soc.*, **1956**, 3181.

¹¹⁰ Baker and Howes, *J. Chem. Soc.*, **1953**, 122.

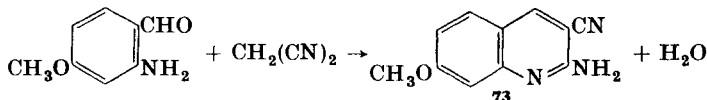
¹¹¹ Schiemenz, *Chem. Ber.*, **95**, 485 (1962).

¹¹² Junek, *Monatsh. Chem.*, **95**, 240 (1964).

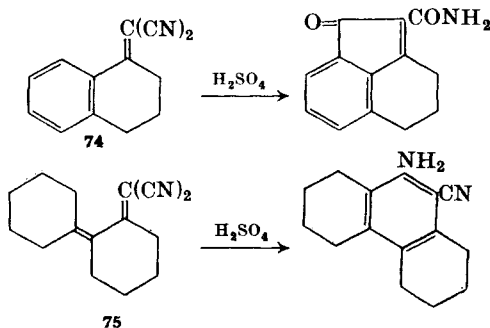
Acetylacetone and benzoylacetone condense with malononitrile to give pyridones.⁹⁹



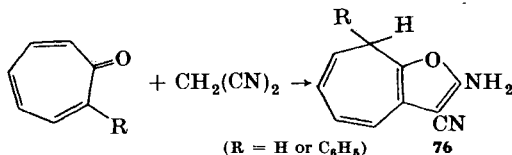
The substituted *o*-aminobenzaldehyde formulated below and malononitrile give the aminoquinoline **73**.¹¹³



There are reports of difficulty in the hydrolysis and reduction of some of the 1,1-dicyanomethylene compounds obtained from malononitrile.^{16,114} To the extent that this proves to be general it will limit their usefulness as intermediates in the synthesis of arylacrylic and arylpropionic acids. Hydrolysis of the tetralin derivative **74** with concentrated sulfuric acid gives an acenaphthenone derivative.¹¹⁵ Similar examples have been given.^{115, 116} In contrast to this, the hydrobiphenyl derivative **75** cyclizes to an octahydrophenanthrenylamine.¹¹⁷



Tropone and 2-phenyltropone react with malononitrile to give the heterocyclic system **76**.¹¹⁸ The cyclohexylidene malononitrile **77**



¹¹³ Troeger and Cohaus, *J. Prakt. Chem.*, [2] **117**, 97 (1927).

¹¹⁴ Battersby, Openshaw, and Wood, *J. Chem. Soc.*, **1953**, 2468.

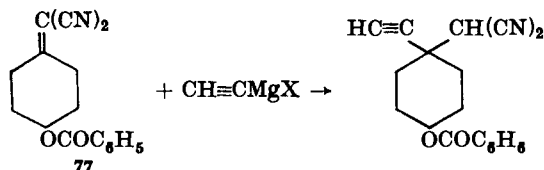
¹¹⁵ Campaigne, Bulbenko, Kreighbaum, and Maulding, *J. Org. Chem.*, **27**, 4428 (1962).

¹¹⁶ Campaigne, Subramanya, and Maulding, *J. Org. Chem.*, **28**, 624 (1963).

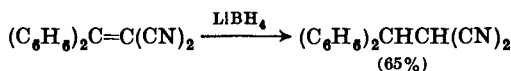
¹¹⁷ Jäger, *Chem. Ber.*, **95**, 244 (1962).

¹¹⁸ Nozoe, Mukai, and Suzuke, *Bull. Chem. Soc. Japan*, **36**, 41 (1963) [*C.A.*, **59**, 1562 (1963)].

undergoes Michael addition with acetylenic Grignard reagents to give 1,1-disubstituted cyclohexanes.¹¹⁹



Reduction of the double bond in the benzophenone malononitrile condensation product has been achieved by lithium borohydride in tetrahydrofuran.⁹⁴



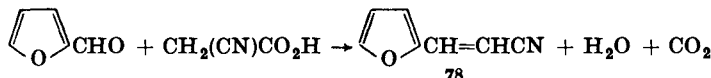
Condensations with Cyanoacetic Acid (Table VI)

The original studies of condensations between cyanoacetic acid and aldehydes or ketones described the formation of α -cyanoacrylic or α -cyanocinnamic acids.¹²⁰⁻¹²² The catalysts used were ammonia and ammonium salts, primary and secondary amines, and their salts. In all cases except two (cyclohexanone and 4-methylcyclohexanone)³⁸ the



α,β -unsaturated compound is reported to be formed, and from some reactions a mixture of *cis* and *trans* isomers is obtained (p. 221).¹²³⁻¹²⁵

α -Cyano α,β -unsaturated acids have also been prepared using ammonium acetate (Cope modification),¹²⁵⁻¹²⁷ amino acids,¹⁰⁶ and weakly basic ion-exchange resins as condensing agents.¹²⁸ Prolonged treatment with ammonium acetate in boiling benzene occasionally leads to formation of an unsaturated nitrile such as 78.¹²⁹ Unsaturated nitriles such as 78



¹¹⁹ Ramage and Parker, *J. Org. Chem.*, **28**, 1723 (1963).

¹²⁰ Knoevenagel, Ger. pat. 156,560 (*Chem. Zentr.*, **1905**, I, 56).

¹²¹ Knoevenagel, Ger. pat. 164,296 (*Chem. Zentr.*, **1905**, II, 1701).

¹²² Knoevenagel, Ger. pat. 162,281 (*Chem. Zentr.*, **1905**, II, 726).

¹²³ Schiemenz, *Angew. Chem.*, **72**, 578 (1960).

¹²⁴ Schiemenz and Engelhard, *Chem. Ber.*, **93**, 1755 (1960).

¹²⁵ Smit, *Rec. Trav. Chim.*, **80**, 898 (1961).

¹²⁶ Whyte and Cope, *J. Am. Chem. Soc.*, **65**, 2002 (1943).

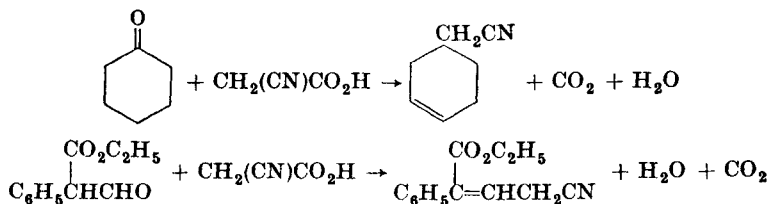
¹²⁷ Cope, D'Addieco, Whyte, and Glickman, *Org. Syntheses*, Coll. Vol. **4**, 234 (1963).

¹²⁸ Astle and Gergel, *J. Org. Chem.*, **21**, 493 (1956).

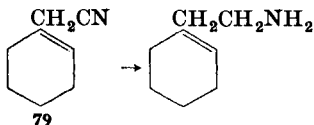
¹²⁹ Patterson, *Org. Syntheses*, **40**, 46 (1960).

are the main products when pyridine or a mixture of pyridine and piperidine is used as the catalyst with equimolar amounts of carbonyl compound and cyanoacetic acid.⁶⁷ Aromatic aldehydes or ketones may furnish a mixture of the *cis*- and *trans*-cinnamonitriles in which the *trans* isomer usually predominates. It has been shown that of the *cis*- and *trans*- α -cyanocinnamic acids formed initially in the condensation from 3,4,5-trimethoxybenzaldehyde only the *cis* acid is readily decarboxylated to the *trans*-cinnamonitrile (see p. 221).

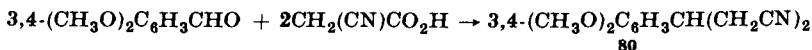
Aliphatic aldehydes and ketones frequently yield the β,γ -unsaturated nitrile or a mixture of α,β - and β,γ -isomers.¹³⁰ If geometric isomers are also present the mixture is difficult to separate, but separation is unnecessary if the mixture is to be hydrogenated to the saturated nitrile. The β,γ -isomer appears to predominate in the nitriles derived from cyclic ketones such as cyclohexanone¹³¹ and in products in which the β,γ double bond is conjugated with a benzene ring or with an ester group.¹³² Nitriles can also be obtained by decarboxylation of the initially formed cyano acids.¹²⁶



The nitrile **79** has been reduced by Raney nickel or lithium aluminum hydride to β -(1-cyclohexenyl)ethylamine.¹³¹



A third class of compounds, glutaronitriles such as **80**, is formed if excess cyanoacetic acid is used in the piperidine-pyridine catalyzed condensation at 100° or over.¹³³



It has been pointed out that condensations between cyanoacetic acid and benzaldehyde or 2,4-dichlorobenzaldehyde lead to some glutaric acid

¹³⁰ Baerts, *Bull. Soc. Chim. Belges*, **41**, 314 (1932).

¹³¹ Schnider and Hellerbach, *Helv. Chim. Acta*, **33**, 1443 (1950).

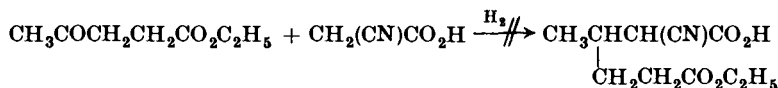
¹³² Borsche and Niemann, *Ber.*, **69**, 1995 (1936).

¹³³ Schiemenz and Engelhard, *Chem. Ber.*, **95**, 196 (1962).

dinitriles, even when equimolar quantities of reagents are used, whereas 3-methoxy-4-hydroxybenzaldehyde gives only the unsaturated nitrile even with a 3:1 ratio of cyanoacetic acid to aldehyde.¹³³

Recent experiments have shown that acetals of aromatic aldehydes will condense with cyanoacetic acid, with or without a basic catalyst.¹³⁴

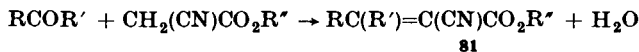
The unsaturated α -cyano acids can be reduced to saturated α -cyano acids and the unsaturated nitriles to unsaturated or saturated amines. However, an attempt to displace the equilibrium in the condensation between ethyl levulinate and cyanoacetic acid by simultaneous hydrogenation was unsuccessful.¹³⁵ (See p. 243 for a successful use of this technique with cyanoacetic esters.)



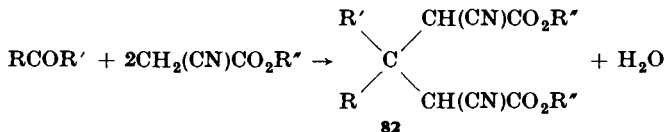
Unidentified abnormal products were obtained from the condensation of cyanoacetic acid with acetylacetone, ethoxyacetoacetic ester, and phloroglucinol.¹³⁶ No condensation was achieved with benzoquinone.

Condensations with Cyanoacetic Esters (Table VII)

The normal products of condensation between cyanoacetic esters and aldehydes or ketones are α,β -unsaturated cyanoacetates, **81**. If excess cyanoacetic ester is used, substituted glutaric esters, **82**, can be obtained. The most consistently successful catalysts for the condensations involving ketones have been ammonium acetate or acetamide with acetic acid and a water-immiscible solvent to remove the water formed in the condensation by azeotropic distillation (Cope modification).^{46, 47}



81



82

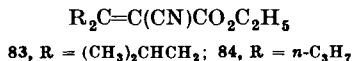
The yield of product and the rate of reaction vary with the degree of steric hindrance in the ketone. Under the same conditions the ester **83**

¹³⁴ Klein and Meyer, *J. Org. Chem.*, **29**, 1035 (1964).

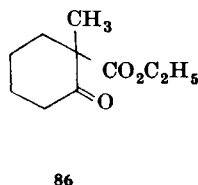
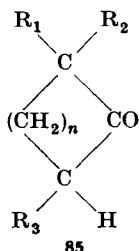
¹³⁵ Stevens, *J. Chem. Soc.*, **1960**, 1121.

¹³⁶ Shemyakin and Trakhtenberg, *J. Gen. Chem. USSR (English Transl.)*, **13**, 553 (1943) [*C.A.*, **39**, 497 (1945)].

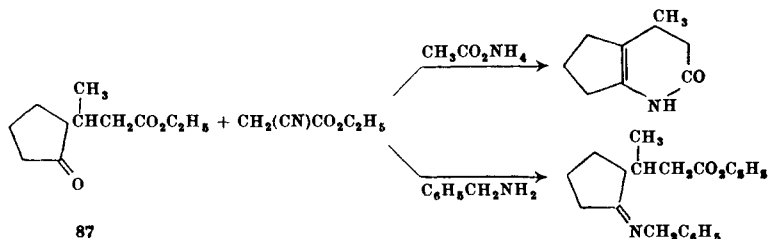
was obtained in 40% yield from diisobutyl ketone and the ester **84** in 80% yield from di-*n*-propyl ketone.⁴⁷



It is reported that good yields can be obtained from unreactive ketones such as benzophenone if the ammonium acetate catalyst is added in portions.¹³⁷ Other examples of steric hindrance are furnished by the cycloalkanones **85**, *n* = 2 or 3.¹³⁸ With piperidine at room temperature, condensation occurred readily only with the ketones that had a single α substituent. With two α-substituents, e.g., R₁ = CH₃ and R₂ = CO₂C₂H₅ only 3% conversion was achieved after 8 months. Similar compounds carrying two α-substituents have, however, been successfully condensed with ethyl cyanoacetate by using ammonium acetate in boiling benzene. An example is the cyclohexanone **86**.¹³⁹ The cyclopentanone **87** and



ethyl cyanoacetate with ammonium acetate as catalyst furnish a pyridone. With benzylamine as catalyst the Schiff base is formed.¹⁴⁰



In condensations involving aldehydes the commonest catalyst is an amine (usually piperidine) in alcoholic solution, but numerous examples of the application of the Cope modification are also available. Weakly

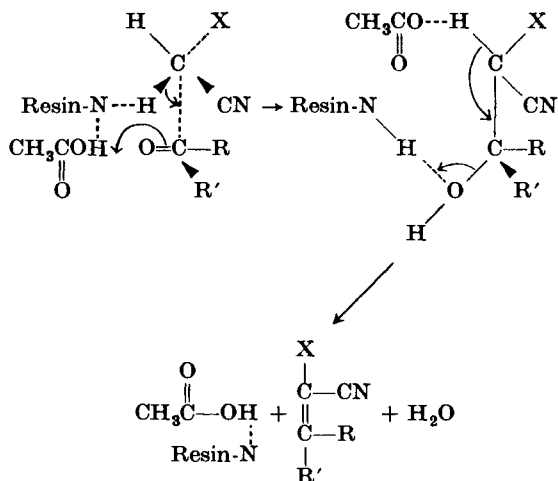
¹³⁷ Cragoe, Robb, and Sprague, *J. Org. Chem.*, **15**, 388 (1950).

¹³⁸ Barrett, Cook, and Linstead, *J. Chem. Soc.*, **1935**, 1065.

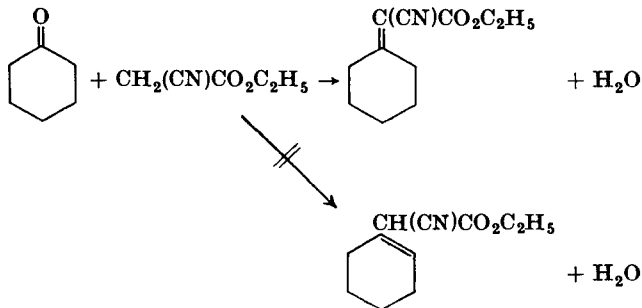
¹³⁹ Chatterjee and Bhattacharyya, *J. Indian Chem. Soc.*, **34**, 520 (1957).

¹⁴⁰ Dev, *J. Indian Chem. Soc.*, **30**, 443 (1953).

basic ion-exchange resins in the acetate form have also been used as catalysts, but differences in relative rates of condensation are observed from those obtained with piperidinium acetate. Cyclohexanone condenses much faster than methyl ethyl ketone in the presence of piperidinium acetate,¹⁴¹ whereas the rates are almost the same with Dowex 3 acetate. It is suggested that the resin-catalyzed condensation involves a transition state in which steric hindrance is less important, as shown in the formulation.¹⁴¹



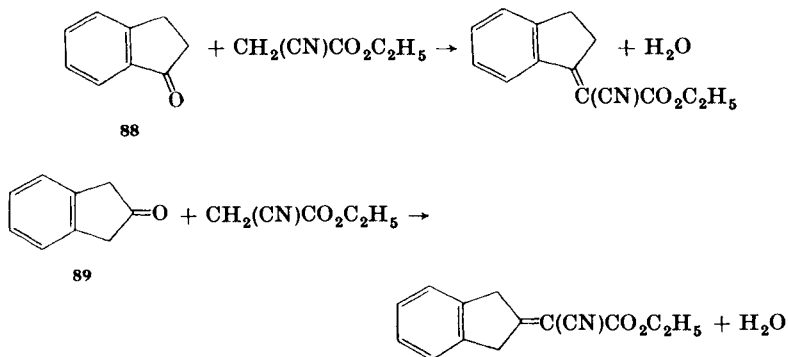
The position of the double bond in the unsaturated condensation products is now generally accepted as α,β to the ester group,^{46, 142} rather than β,γ as was originally suggested.³⁸



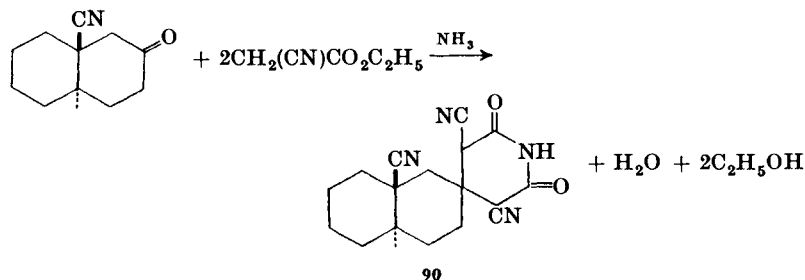
¹⁴¹ Hein, Astle, and Shelton, *J. Org. Chem.*, **26**, 4874 (1961).

¹⁴² Vargha and Mester, *Studia Univ. Babes-Bolyai, Ser. Chem.*, No. 1, 127 (1962) [*C.A.*, **61**, 2983 (1964)].

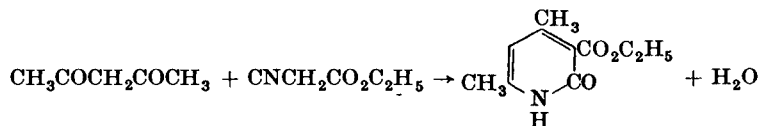
The indanones **88** and **89** are reported to react with ethyl cyanoacetate to give indene derivatives;¹⁴³ these have been shown to be the indanylidene derivatives formulated in the accompanying equations.^{143a}



If alcoholic ammonia is used in the condensation of ketones with cyanoacetic ester, a glutarimide is formed, e.g., **90**,¹⁴⁴ possibly via the *bis*-(cyanoacetamide) derivative.



Pyridine derivatives have also been reported from the condensation between cyanoacetic esters and 1,3-diketones. The reaction with acetylacetone is illustrated.¹⁴⁵



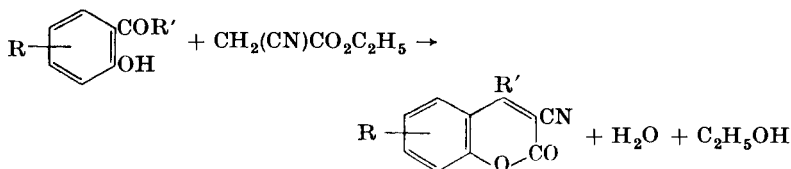
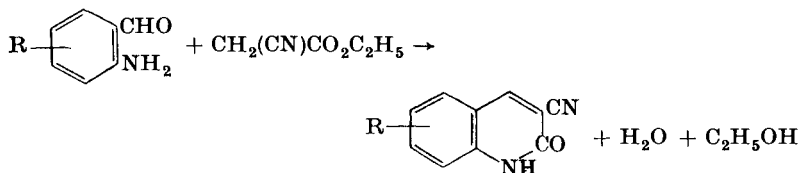
¹⁴³ Ingold and Thorpe, *J. Chem. Soc.*, **115**, 150, 156 (1919).

^{143a} G. Jones and W. J. Rae, unpublished observations.

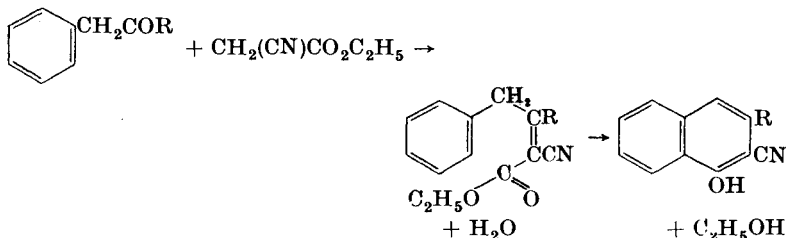
¹⁴⁴ Haworth, Hutley, Leach, and Rodgers, *J. Chem. Soc.*, **1962**, 2726.

¹⁴⁵ Simonsen and Nayak, *J. Chem. Soc.*, **107**, 794 (1915).

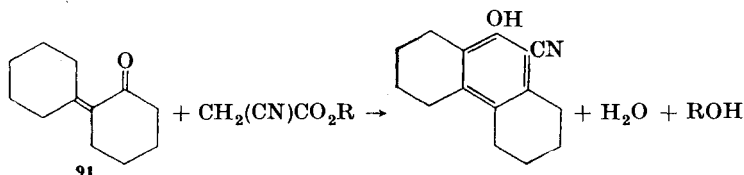
o-Aminobenzaldehydes give carbostyris,¹¹³ and *o*-hydroxybenzaldehydes^{146, 147} and *o*-hydroxyarylkones¹⁴⁸ give 3-cyanocoumarins.



An unusual cyclization occurs when benzyl ketones condense with cyanoacetic esters in the presence of ammonium acetate at temperatures between 120° and 180°. The unsaturated compound initially formed cyclizes to an α -naphthol derivative.¹⁴⁹



In similar fashion the ketone **91** gives a hydrophenanthrol.¹¹⁷



Acetals of aromatic aldehydes will condense with cyanoacetic esters either catalyzed or uncatalyzed, although in most of the experiments reported a mixture of cyanoacetic acid and ester was used.¹³⁴

In many syntheses the desired product has been the saturated cyano ester resulting from reduction of the acrylic or cinnamic ester first formed.

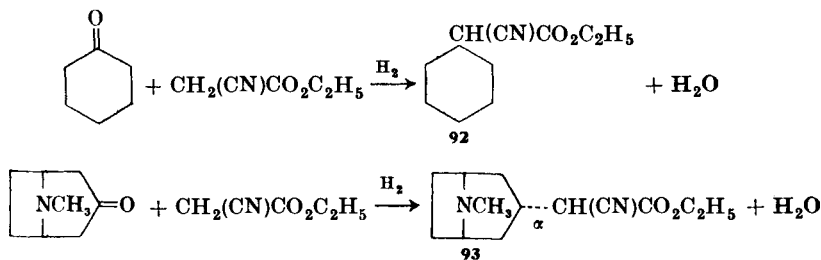
¹⁴⁶ Horning and Horning, *J. Am. Chem. Soc.*, **69**, 968 (1947).

¹⁴⁷ Cingolani, *Gazz. Chim. Ital.*, **84**, 848 (1954).

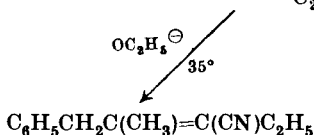
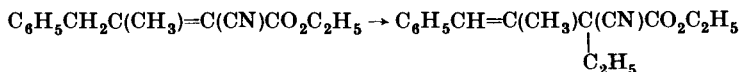
¹⁴⁸ Wiener, Schroder, and Link, *J. Am. Chem. Soc.*, **79**, 5303 (1957).

¹⁴⁹ Fiesselmann and Ehmman, *Chem. Ber.*, **91**, 1709 (1958).

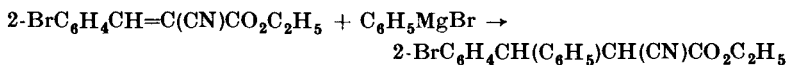
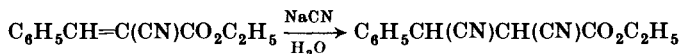
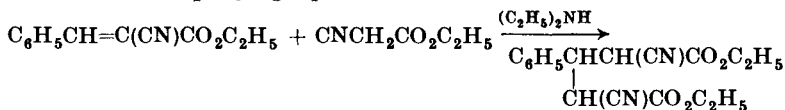
Very satisfactory yields of the saturated compounds can be obtained by simultaneous condensation and reduction.¹⁵⁰ The most common solvent is ethanol, and a mixture of ammonium acetate and acetic acid with palladium on charcoal provides catalysis for condensation and reduction. In some cases, as in the synthesis of the ester **92**, room temperature is sufficient,¹⁵⁰ but in others higher temperatures are necessary, as in the synthesis of the ester **93**.¹⁵¹ Selective reduction of the double bond has also been achieved by hydrides under suitable conditions.⁹⁴



The α -cyano acrylates obtained in the condensations between carbonyl compounds and cyanoacetic esters undergo a number of useful transformations. Some on treatment with ethoxide under mild conditions give acrylonitriles.¹⁵² The double bond is sufficiently activated to add



Michael donors,¹⁵³ cyanide ion,¹⁵⁴ or Grignard reagents.¹⁵⁵ Examples are given in the accompanying equations.



¹⁵⁰ Alexander and Cope, *J. Am. Chem. Soc.*, **66**, 886 (1944).

¹⁵¹ Zirkle, Anderson, Gerns, Indik, and Pavloff, *J. Org. Chem.*, **27**, 1279 (1962).

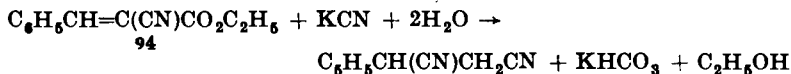
¹⁵² Hugh and Kon, *J. Chem. Soc.*, **1930**, 780.

¹⁵³ Palit, *J. Indian Chem. Soc.*, **14**, 219 (1937).

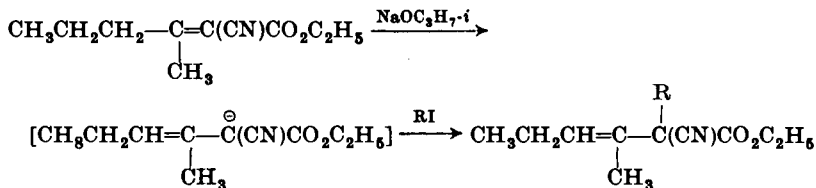
¹⁵⁴ Baker and Leeds, *J. Chem. Soc.*, **1948**, 977.

¹⁵⁵ Newman and Phillips, *J. Am. Chem. Soc.*, **81**, 3668 (1959).

The ester **94** heated under reflux with aqueous ethanolic potassium cyanide is reported to give phenylsuccinonitrile in good yield.¹⁵⁶

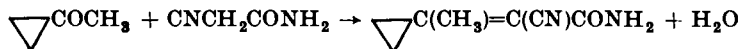


Alkylation of alkylidenecyanoacetic esters proceeds readily to give the β,γ -unsaturated esters.¹⁵⁷

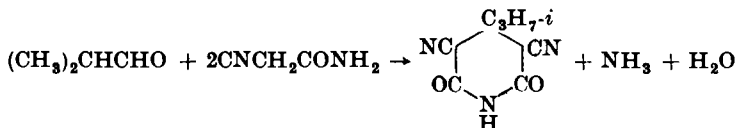
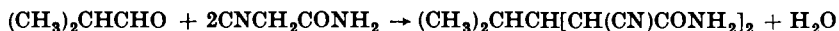


Condensations with Cyanoacetamides (Table VIII)

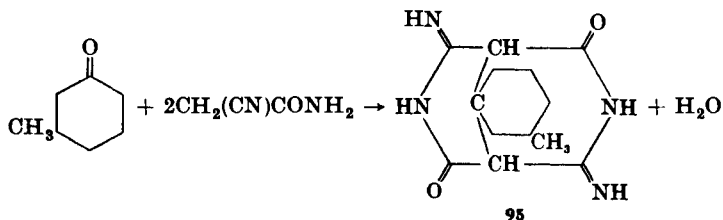
Cyanoacetamides condense with aldehydes or ketones to give α -cyanoacrylamides.¹⁵⁸



It is also possible to obtain *bis*-(cyanoacetamides) which may cyclize to glutarimides.¹⁵⁹



A less common cyclization to the tricyclic compound **95** has been reported in the condensation between cyanoacetamide and 3-methylcyclohexanone.¹⁶⁰



¹⁵⁶ Mowry, *J. Am. Chem. Soc.*, **68**, 2108 (1946).

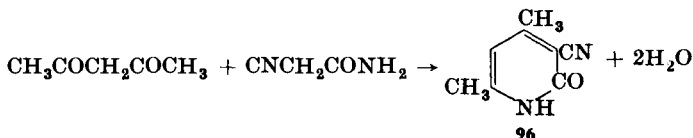
¹⁵⁷ Cope and Hancock, *J. Am. Chem. Soc.*, **60**, 2903 (1938).

¹⁵⁸ Opie, Seifter, Bruce, and Mueller, U.S. pat. 2,538,322 [C.A., **45**, 6657 (1951)].

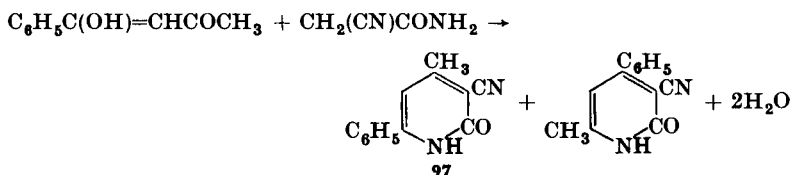
¹⁵⁹ Curtis, Day, and Kimmins, *J. Chem. Soc.*, **123**, 3134 (1923).

¹⁶⁰ Thorpe and Wood, *J. Chem. Soc.*, **103**, 1586 (1913).

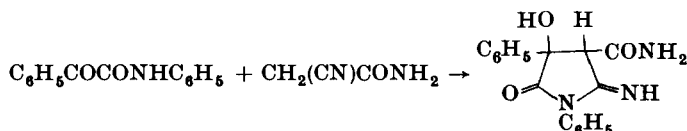
When 1,3-diketones are condensed with cyanoacetamide, a 1:1 condensation gives a pyridone. Acetylacetone gives the pyridone **96**.¹⁶¹



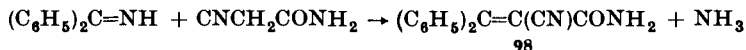
With unsymmetrical β -diketones the condensation occurs in the direction which implies that Knoevenagel condensation (rather than Michael addition to the enol) is the first step. Thus benzoylacetone, which enolizes as shown, condenses to give the pyridone **97** as the major product.¹⁶²



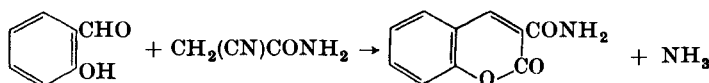
Benzoylformanilide condenses with cyanoacetamide to give a pyrrolidone imine.¹⁶³



An observation which may bear on the mechanism of the Knoevenagel condensation is that the condensation of benzophenone imine with cyanoacetamide occurs without a catalyst at 115° to give a quantitative yield of the amide **98**.¹⁶⁴



Condensation of salicylaldehyde with cyanoacetamide gives a coumarin derivative.¹¹¹



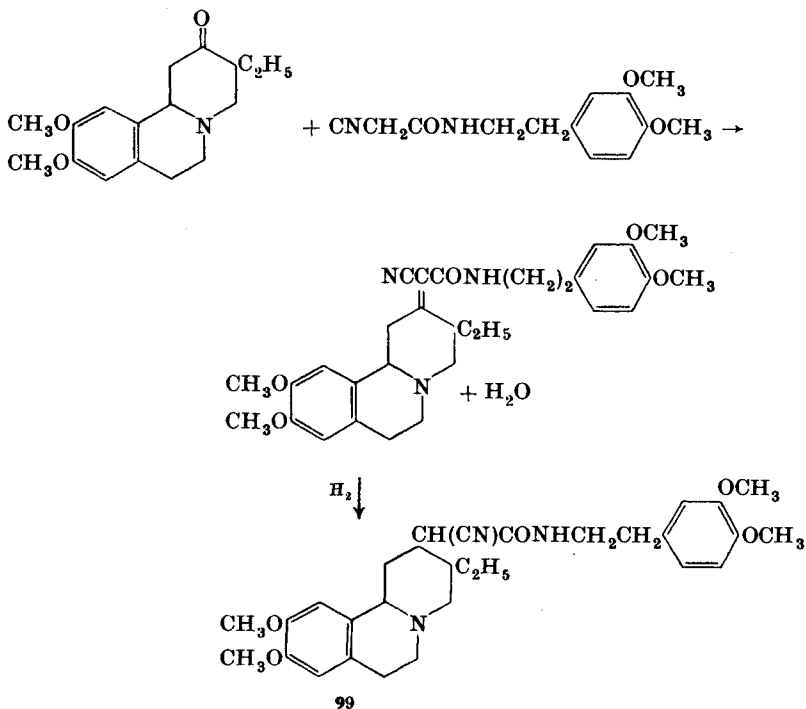
¹⁶¹ Wagtendonk and Wibaut, *Rec. Trav. Chim.*, **61**, 728 (1942).

¹⁶² Bardhan, *J. Chem. Soc.*, **1929**, 2223.

¹⁶³ Scudi and Lindwall, *J. Am. Chem. Soc.*, **57**, 1647 (1935).

¹⁶⁴ Charles, *Compt. Rend.*, **242**, 2468 (1956).

The α -cyano acrylamides formed by the normal condensation with cyanoacetamide and its derivatives are often readily reduced to the corresponding saturated compounds. The reduction product **99**, shown in the accompanying formulation, is an intermediate in the synthesis of emetine derivatives.¹¹⁴



Condensations with Ketones (Tables IX and X)

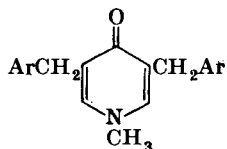
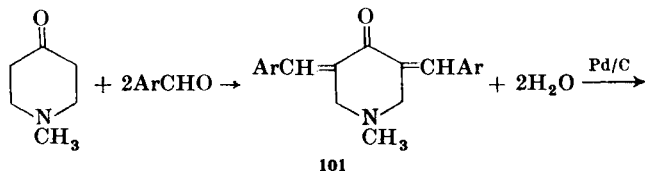
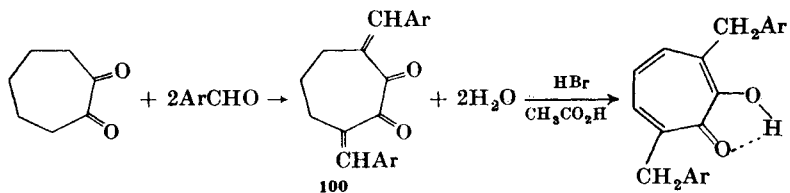
Condensations involving an aldehyde as the carbonyl component and a ketone as the active methylene component are commonly catalyzed by strong bases, but some of these condensations can be effected under the conditions of the Knoevenagel condensation.

Examples are the preparation of the arylidene ketones **100** and **101**, which were isomerized to tropolones^{165,166} and pyridones,¹⁶⁷ respectively.

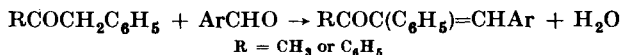
¹⁶⁵ Leonard and Robinson, *J. Am. Chem. Soc.*, **75**, 2146 (1953).

¹⁶⁶ Leonard and Berry, *J. Am. Chem. Soc.*, **75**, 4991 (1953).

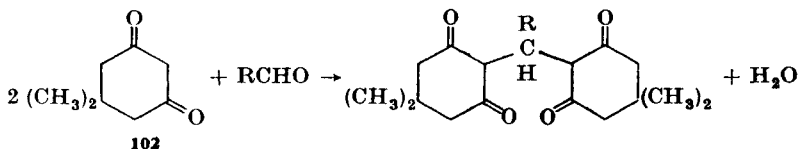
¹⁶⁷ Leonard and Locke, *J. Am. Chem. Soc.*, **77**, 1855 (1955).



The simple ketones which condense readily under the conditions of the Knoevenagel reaction usually have additional activation on the methylene group provided by a phenyl group. Desoxybenzoin condenses readily with aromatic aldehydes to give substituted stilbenes,¹⁶⁸ as does methyl benzyl ketone.⁶⁹



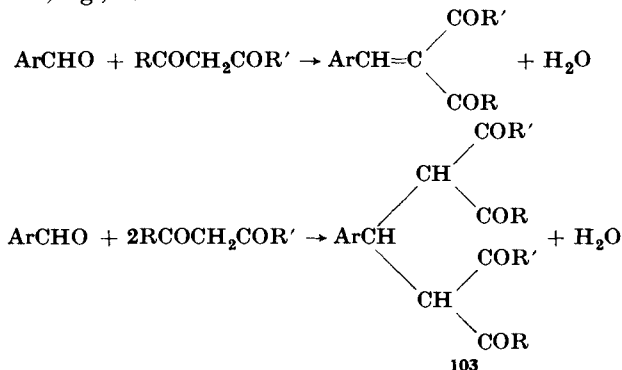
1,3-Diketones are highly reactive in Knoevenagel condensations with aldehydes. This reactivity is the basis of one procedure for the characterization of aldehydes; dimedone, 102, reacts with aldehydes but not ketones to form bis condensation products which are generally crystalline. The condensation is sometimes performed with piperidine as catalyst,¹⁶⁹ but also frequently with acetic acid, and therefore falls only peripherally within the scope of this chapter.



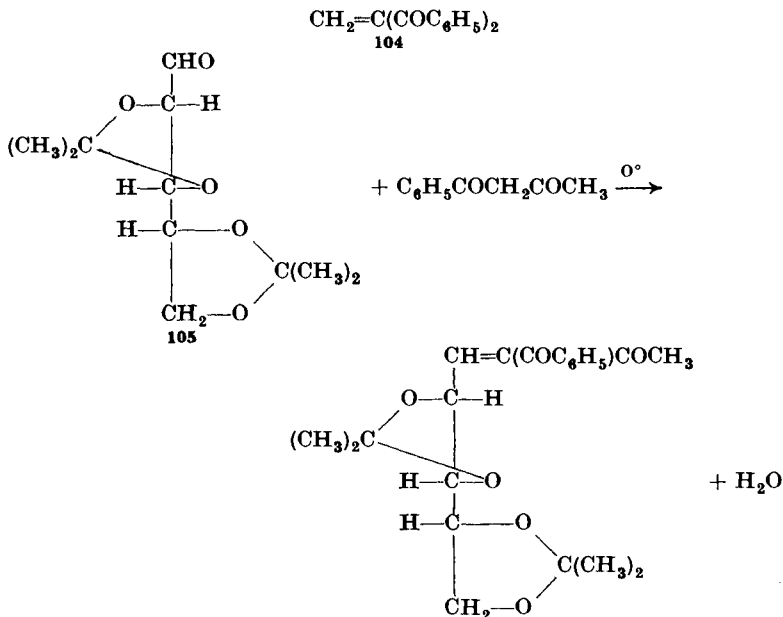
¹⁶⁸ Dornow and Boberg, *Ann.*, **578**, 107 (1952).

¹⁶⁹ Horning and Horning, *J. Org. Chem.*, **11**, 98 (1946).

Aromatic aldehydes condense with 1,3-diketones at 0° to give arylidene derivatives^{81, 170} and at higher temperatures to give derivatives of 1,5-diketones, e.g., **103**.¹⁷¹



Simple aliphatic aldehydes usually give the 1,5-diketone derivative such as **103**.¹⁷² Formaldehyde and dibenzoylmethane furnish the methylene diketone **104**.¹⁷³ The D-arabinose derivative **105** condenses with benzoylacetone to give the unsaturated diketone.¹⁷⁴



¹⁷⁰ Knoevenagel and Arnot, *Ber.*, **37**, 4496 (1904).

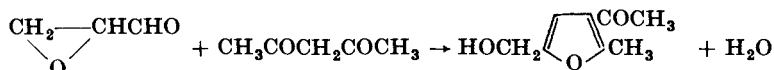
¹⁷¹ Martin, Shamma, and Fernelius, *J. Am. Chem. Soc.*, **80**, 5852 (1958).

¹⁷² Knoevenagel, *Ber.*, **36**, 2136 (1903).

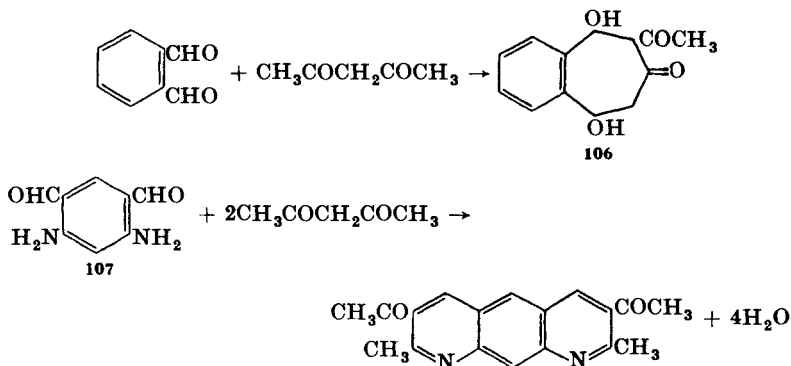
¹⁷³ Cannon, Santilli, and Shenian, *J. Am. Chem. Soc.*, **81**, 1666 (1959).

¹⁷⁴ Zinner, Wittenburg, and Rembarz, *Chem. Ber.*, **92**, 1616 (1959).

Acetylacetone condenses with glycidaldehyde to give a furan derivative¹⁷⁵

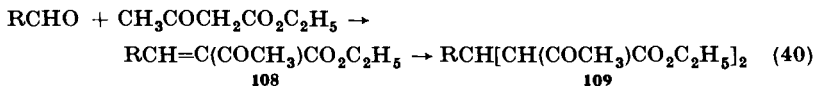


with phthalaldehyde to yield the benzotropone derivative **106**,¹⁷⁶ and with the diaminoisophthalaldehyde **107** to furnish a pyridoquinoline derivative.¹⁷⁷



Condensations with β -Ketonic Esters (Tables XI and XII)

In the Hantzsch pyridine synthesis two molecules of a β -ketonic ester react with one of an aldehyde and one of ammonia. The 1,5-diketones, **109**, isolated as by-products are the normal products when amine catalysts are used at room temperature or above.^{3, 178, 179} By chilling the reaction mixture it is possible to isolate in good yield the alkylidene- or arylidene-acetoacetates,^{5, 6} **108**, which presumably represent the first stage in the condensation. It was the study of these condensations which led Knoevenagel to the general reaction which forms the subject of this chapter.



The best catalyst for the preparation of unsaturated products such as **108** is a secondary amine at 0°. With an amine acetate or caproate⁶⁹ or

¹⁷⁵ Williams, Payne, Sullivan, and Vaness, *J. Am. Chem. Soc.*, **82**, 4885 (1960).

¹⁷⁶ Davey and Gottfried, *J. Org. Chem.*, **26**, 3703 (1961).

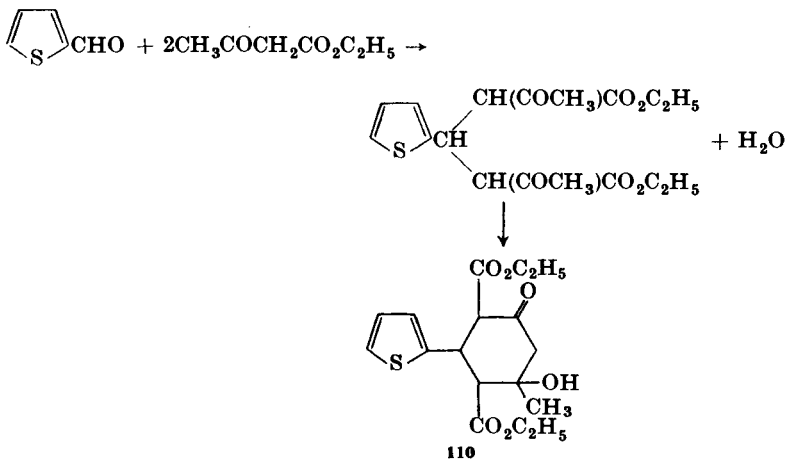
¹⁷⁷ Ruggli, Hindermann, and Frey, *Helv. Chim. Acta*, **21**, 1074 (1938).

¹⁷⁸ Knoevenagel, *Ann.*, **288**, 321 (1896).

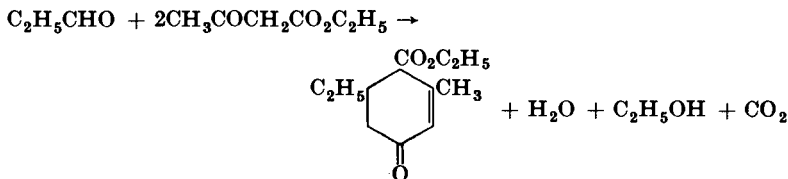
¹⁷⁹ Smith and Kort, *J. Am. Chem. Soc.*, **72**, 1878 (1950).

an ion-exchange resin^{180, 181} a higher reaction temperature can be used, but the yields are generally smaller than with the secondary amine catalyst.¹⁸² The use of secondary amine catalysts at room temperature or above gives the 1,5-diketones **109** in good yield.^{179, 183}

The 1,5-diketones can cyclize to cyclohexanones such as **110**.¹⁸⁴ Such



cyclizations can be effected in high yields by treatment of the crude 1,5-diketone intermediates with acetic acid and sulfuric acid. The products are cyclohexenones.¹⁸⁵ The cyclizations described in this paragraph should be compared with those in Chapter 1 of this volume.



Salicylaldehydes react readily with β -ketonic esters to give 3-acylcoumarins.⁹¹ α -Hydroxy ketones (acyloins) give acylfuranones, and β -hydroxy aldehydes (aldols) give dihydropyranones.¹⁸⁶

¹⁸⁰ Mastagli and Andrie, *Bull. Soc. Chim. France*, **1957**, 792.

¹⁸¹ Astle and Zaslowky, *Ind. Eng. Chem.*, **44**, 2867 (1952).

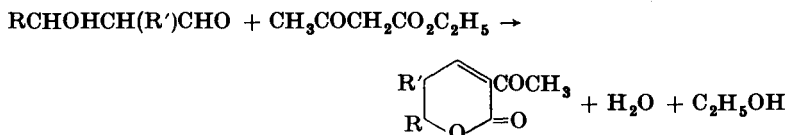
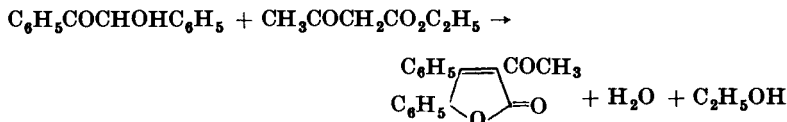
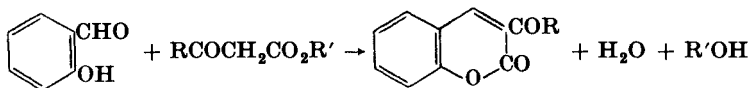
¹⁸² Cope and Hofmann, *J. Am. Chem. Soc.*, **63**, 3456 (1941).

¹⁸³ Smith and Shelton, *J. Am. Chem. Soc.*, **76**, 2732 (1954).

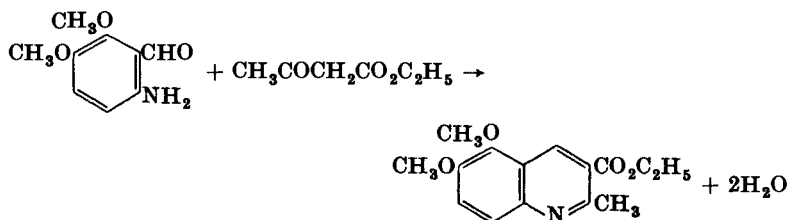
¹⁸⁴ Miller and Nord, *J. Org. Chem.*, **16**, 1726 (1951).

¹⁸⁵ Horning, Denekas, and Field, *J. Org. Chem.*, **9**, 549 (1944).

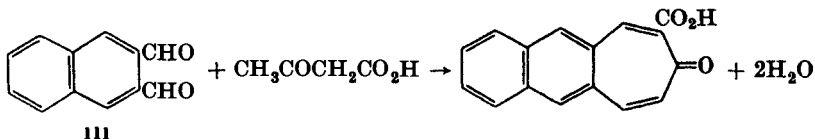
¹⁸⁶ Lacey, *J. Chem. Soc.*, **1954**, 822.



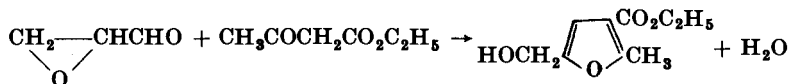
o-Aminobenzaldehydes and ethyl acetoacetate give quinaldine-3-carboxylic acid derivatives.¹⁸⁷



A similar reaction with the anil of *o*-aminobenzaldehyde gives ethyl quinaldine-3-carboxylate.¹⁸⁸ An aromatic ortho dialdehyde such as the naphthalene derivative 111 has been reported to give a 2,3-naphthotropone when condensed with acetoacetic acid.¹⁸⁹



As in its reaction with acetylacetone (p. 249), glycidaldehyde with ethyl acetoacetate forms a furan derivative.¹⁷⁵

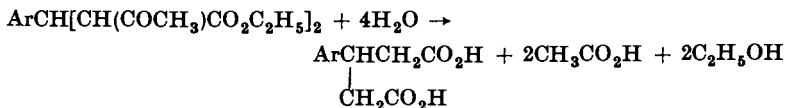


¹⁸⁷ Borsche and Ried, *Ber.*, **76**, 1013 (1943).

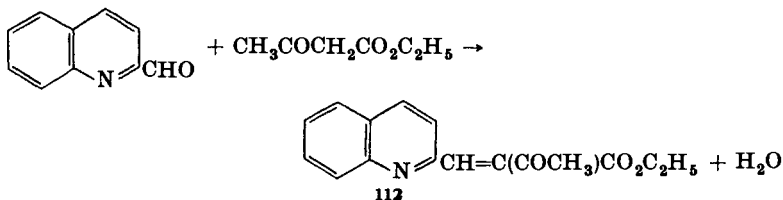
¹⁸⁸ Borsche, Doeller, and Wagner-Roemmich, *Ber.*, **76**, 1101 (1943).

¹⁸⁹ Ried and Schwenecke, *Chem. Ber.*, **91**, 571 (1958).

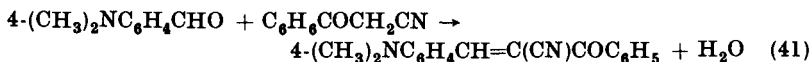
The *bis*-acetoacetates prepared from aromatic aldehydes and ethyl acetoacetate can be hydrolyzed in good yield to the corresponding glutaric acids by heating with alcoholic sodium hydroxide.¹⁷⁹ This



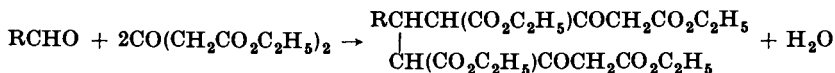
synthesis has been extended to the preparation of glutaric acids containing a heterocyclic group in the β position.¹⁸³ It was reported that attempts to condense ethyl acetoacetate with quinoline-2-carboxaldehyde, 5-nitrofurfural, and indole-3-carboxaldehyde were unsuccessful, but quinoline-2-carboxaldehyde has been condensed with ethyl acetoacetate to give the unsaturated compound **112**.¹⁹⁰



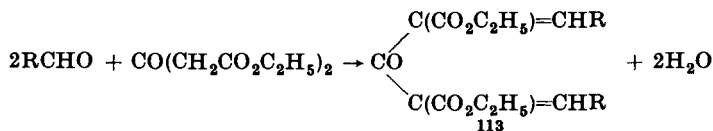
At this point it is convenient to mention condensations using β -ketonic nitriles (dealt with in Table XX) which condense like β -ketonic esters with aldehydes or ketones to give substituted acrylonitriles.¹⁹¹



Acetonedicarboxylic acid and its esters contain two reactive methylene sites, both of which can react with carbonyl compounds leading to a variety of cyclic products. Knoevenagel reported the preparation of a number of aldehyde *bis*-acetonedicarboxylates from benzaldehyde or aliphatic aldehydes and acetonedicarboxylic esters using diethylamine as catalyst at room temperature or below.¹⁷⁸



Two molecules of a sugar such as 4,6-O-benzylideneglucose react with one of diethyl acetonedicarboxylate to give a compound of type **113**.¹⁹²

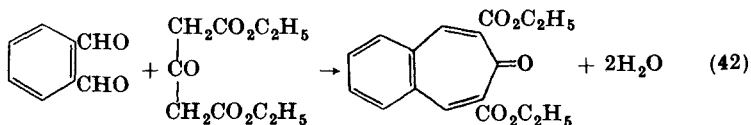


¹⁸⁰ Kloss, *Arch. Pharm.*, **289**, 183 (1956).

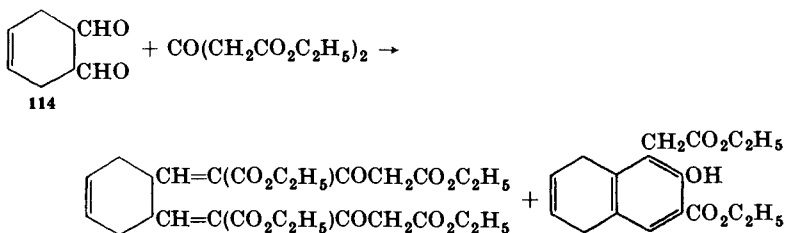
¹⁹¹ Kauffmann, *Ber.*, **50**, 523 (1917).

¹⁹² Papadakis, *J. Org. Chem.*, **20**, 636 (1955).

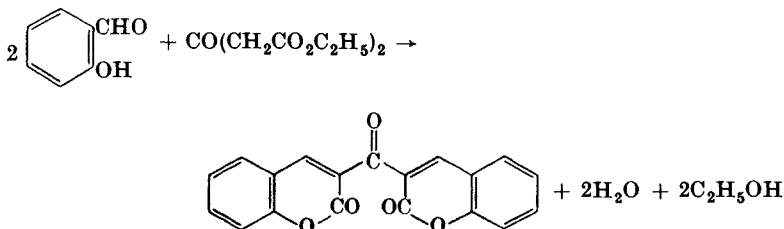
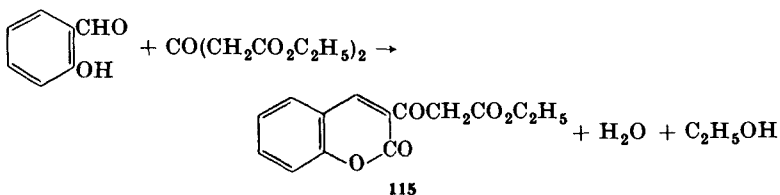
Aromatic *ortho* dicarboxaldehydes like phthalaldehyde react with diethyl acetonedicarboxylate to give tropones.¹⁹³



In contrast, the alicyclic dialdehyde **114** gives a mixture of the cyclohexene and the dihydronaphthalene in which the latter predominates.¹⁹⁴



Salicylaldehyde condenses with an equimolar quantity of diethyl acetonedicarboxylate to give the coumarin **115**. With a 2:1 ratio of aldehyde to ester, the dicoumarinyl ketone is formed.¹⁹⁵



α,β -Unsaturated ketones like benzalacetophenone react with diethyl acetonedicarboxylate forming substituted cyclohexenones.^{196, 197}

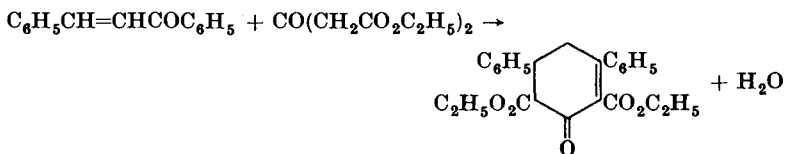
¹⁹³ Thiele and Schneider, *Ann.*, **369**, 287 (1909).

¹⁹⁴ Tarbell and Wargotz, *J. Am. Chem. Soc.*, **76**, 5765 (1954).

¹⁹⁵ Knoevenagel and Langensiepen, *Ber.*, **37**, 4492 (1904).

¹⁹⁶ Deuschel, *Helv. Chim. Acta*, **34**, 180 (1951).

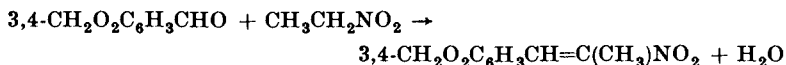
¹⁹⁷ Hanson, *Bull. Soc. Chim. Belges*, **65**, 423 (1956).



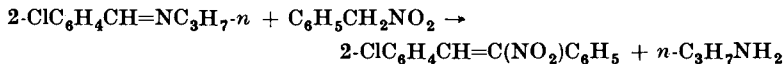
Condensations with Nitro Compounds (Tables XIII and XIV)

Condensations between nitro compounds and ketones or aldehydes can be divided into two classes: those involving an aliphatic nitro compound such as nitromethane or phenylnitromethane, and those involving 2- or 4-nitrotoluenes or similar compounds, in which the electron withdrawal is transmitted through an aromatic ring. Condensations of aliphatic nitro compounds have been reviewed by Hass and Riley.¹⁹⁸ Since there is considerable difference in reactivity, the two groups will be dealt with separately here.

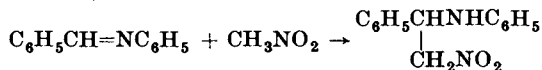
Condensations involving nitromethane, nitroethane, and other aliphatic nitro compounds were performed by Knoevenagel and Walter, who reported that nitrostyrenes were obtained in good yield by the use of a primary amine, or a primary amine salt and sodium carbonate.¹⁹⁹



Secondary and tertiary amines were unsatisfactory, giving slow reactions and poor yields. Worrall, in an extensive study of the catalytic effect of a number of amines, found amylamine the most satisfactory, but in some cases obtained better yields with tertiary amines.²⁷ He suggested that primary amines gave a Schiff base intermediate, whereas secondary and tertiary amines reacted by the Hann and Lapworth mechanism, giving sometimes the β -hydroxy nitro compounds. Evidence for these views has been provided by the successful condensation of Schiff bases with nitromethane and phenylnitromethanes in the absence of a basic catalyst to give good yields of nitrostyrenes.²⁸



In ethanol the product of addition of the nitro compound to the Schiff base can be obtained.^{200, 201}



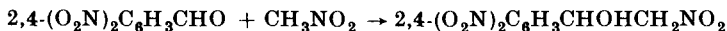
¹⁹⁸ Hass and Riley, *Chem. Rev.*, **32**, 373 (1943).

¹⁹⁹ Knoevenagel and Walter, *Ber.*, **37**, 4502 (1904).

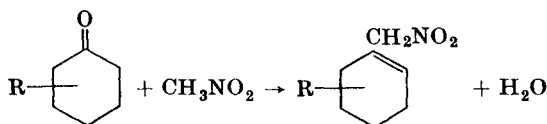
²⁰⁰ Hurd and Strong, *J. Am. Chem. Soc.*, **72**, 4814 (1950).

²⁰¹ Leonard, Leubner, and Burk, *J. Org. Chem.*, **15**, 981 (1950).

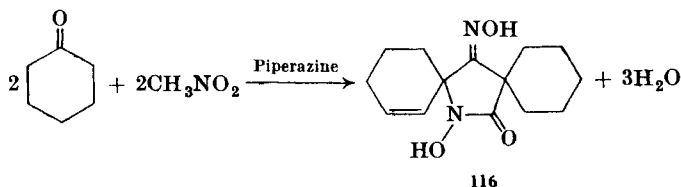
Several examples have been reported of the isolation of β -hydroxy nitro compounds.^{41, 202, 203} It has been suggested that the hydroxy compound is stabilized by the electron-withdrawing effect of the nitro groups.⁴¹ The condensation was catalyzed by triethylamine. Worrall



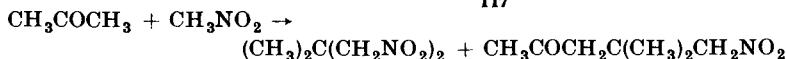
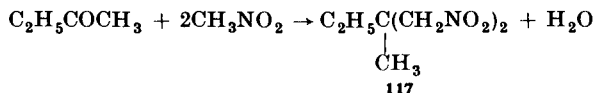
has reported that as a general rule secondary and tertiary amines are more likely to give β -hydroxy nitro compounds. Most of the condensations involve the use of aromatic aldehydes, the products being nitrostyrenes or stilbenes. There are no examples of condensations involving aromatic ketones. Condensations of aliphatic ketones with nitro compounds give low yields and, in many cases, mixtures of products. Condensations of cyclohexanones with nitromethane give the cyclohexenyl nitromethanes.²⁰⁴



Cyclohexanone and a number of other alicyclic ketones also condense with nitromethane (but not with other nitro alkanes) to give compounds such as **116**.^{205, 206} The products from acyclic ketones are commonly



dinitropropane derivatives such as **117** together with the nitroethylene.^{40, 207} Acetone gives a mixture of the dinitropropane and the nitro ketone.²⁰⁸



²⁰² Johnson and Hamilton, *J. Am. Chem. Soc.*, **63**, 2865 (1941).

²⁰³ Rodionov, Alekseeva, and Vleduts, *J. Gen. Chem. USSR (English Transl.)*, **27**, 734 (1957) [*C.A.*, **51**, 16474 (1957)].

²⁰⁴ Nightingale, Erickson, and Shackelford, *J. Org. Chem.*, **17**, 1006 (1952).

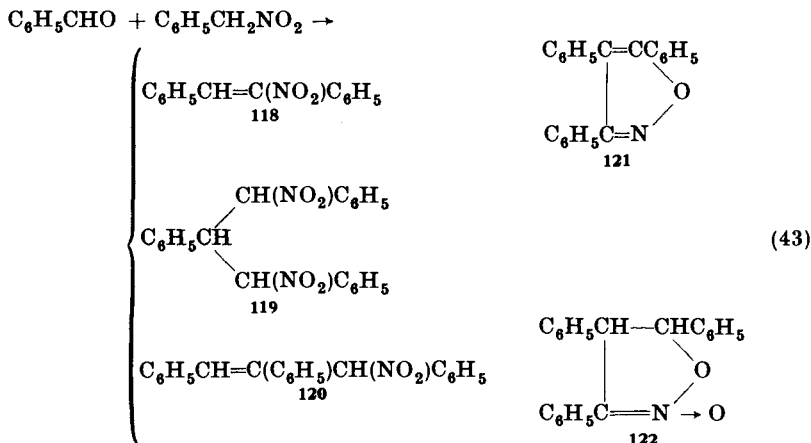
²⁰⁵ Nightingale, Miki, Heintz, and Reich, *J. Org. Chem.*, **28**, 645 (1963).

²⁰⁶ Noland and Sundberg, *J. Org. Chem.*, **28**, 3150 (1963).

²⁰⁷ Lambert and Lowe, *J. Chem. Soc.*, **1947**, 1517.

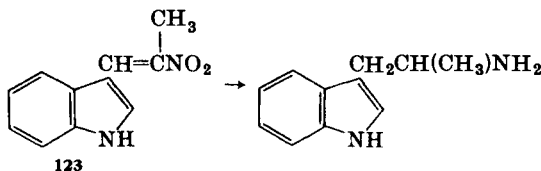
²⁰⁸ Hass and Bourland, U.S. pat. 2,343,256 [*C.A.*, **38**, 2969 (1944)].

Complex by-products have been isolated from condensations involving phenylnitromethane. Benzaldehyde and phenylnitromethane give both *cis*- and *trans*-nitrostilbene **118** and four other products, the dinitropropane **119**, the unsaturated nitro compound **120**, the isoxazole **121**,⁶⁴ and the

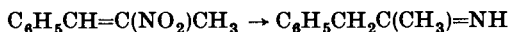


oxide **122**.²⁰⁹ Similar compounds have been obtained from phenylnitromethane and *o*-nitrobenzaldehyde²¹⁰ or *p*-bromobenzaldehyde,²¹¹ and from *p*-methoxyphenylnitromethane and 3,4,5-trimethoxybenzaldehyde.²¹²

The nitrostyrenes provide a good route to β -phenethylamines, since they can be reduced directly to them in good yield by lithium aluminum hydride. The unsaturated indole **123** is reduced to the indolyethylamine.²¹³



When the lithium aluminum hydride is added to the nitro compound (inverse addition), a ketimine may result.²¹⁴



²⁰⁹ Kohler and Barrett, *J. Am. Chem. Soc.*, **46**, 2105 (1924).

²¹⁰ Ruggli and Hegedüs, *Helv. Chim. Acta*, **22**, 407 (1939).

²¹¹ Campbell, Anderson, and Gilmore, *J. Chem. Soc.*, **1940**, 449.

²¹² Rorig, *J. Org. Chem.*, **15**, 394 (1950).

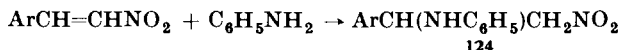
²¹³ Ash and Wragg, *J. Chem. Soc.*, **1958**, 3889.

²¹⁴ Gilsdorf and Nord, *J. Am. Chem. Soc.*, **72**, 4327 (1950).

Addition of bromine to nitrostyrenes gives dibromonitrostyrenes which readily eliminate hydrogen bromide forming β -bromo- β -nitrostyrenes.²¹⁵ The bromine in the bromonitrostyrenes is unreactive.

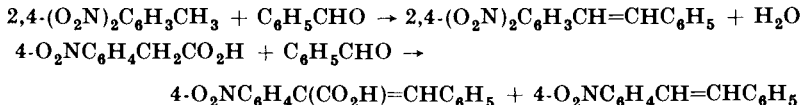


Nitrostyrenes that contain electron-withdrawing substituents in the aromatic ring form addition products such as **124** with organic bases.²⁷

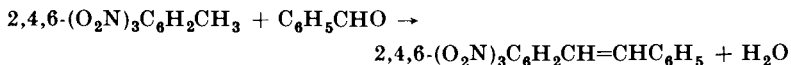


Nitrostilbenes generally do not add amines but do undergo Michael additions (e.g., with dimethyl malonate²¹⁶) as do the nitrostyrenes.⁹⁵

The activating effect of a nitro group *ortho* or *para* to a methylene or methyl group attached to a benzene ring is considerably less than that of one directly attached to the methylene group. Usually two nitro groups are necessary to provide sufficient activation for aromatic aldehydes to condense to give nitrostilbenes. One nitro group provides sufficient activation if the methylene group carries another activating substituent as in *p*-nitrophenylacetic acid.²¹⁷



With three nitro groups present, as in 2,4,6-trinitrotoluene, condensation with aldehydes takes place in ethanol at 40° with a piperidine catalyst.²¹⁸



Comparative studies show that a cyano or sulfonamide group is less effective than a nitro group in activating a methyl group in the *ortho* or *para* position.²¹⁸

Condensations with Sulfonyl and Related Compounds (Tables XV and XVI)

Most of the condensations involving sulfur-containing active methylene components (other than heterocyclic systems such as thiazole) have been

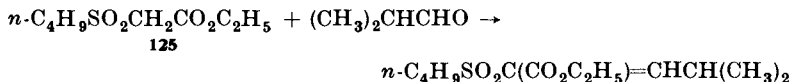
²¹⁵ Worrall, *J. Am. Chem. Soc.*, **62**, 3254 (1940).

²¹⁶ Kohler and Barrett, *J. Am. Chem. Soc.*, **48**, 1773 (1926).

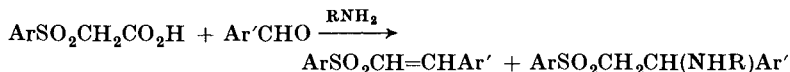
²¹⁷ Baliah and Ganapathy, *J. Indian Chem. Soc.*, **32**, 336 (1955).

²¹⁸ Ullmann and Gschwind, *Ber.*, **41**, 2291 (1908).

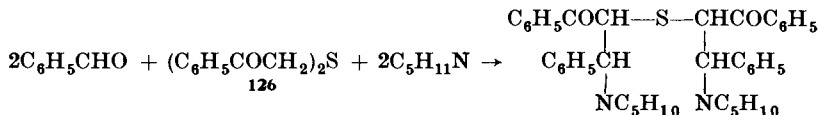
performed with sulfonylacetic acid derivatives or closely related compounds. Thus the sulfonylacetic ester **125** condenses with isobutyraldehyde to give an unsaturated compound.²¹⁹



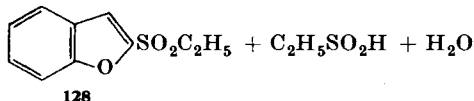
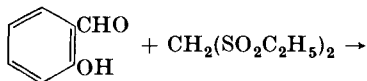
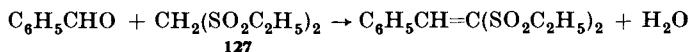
When an arylsulfonylacetic acid is used, the products are the unsaturated compound and the saturated compound formed by addition of one molecule of catalyst to this.²²⁰



Related saturated compounds resulting from addition of the amine catalyst have also been obtained in condensations between *bis*(phenacyl) sulfide (**126**) and aromatic aldehydes.²¹ More recently condensations



between the methylene-*bis*-sulfone **127** and some aldehydes giving 1,1-*bis*-alkylsulfonyl-1-alkenes, have been described. When salicylaldehyde, or substituted salicylaldehydes, were used with piperidine or triethylamine as catalyst, an ethylsulfonylbenzofuran **128** was obtained.²²¹



Miscellaneous Active Methylene Compounds

The major classes of compound dealt with in this section are those in which the activation is provided by an electron-deficient heterocycle

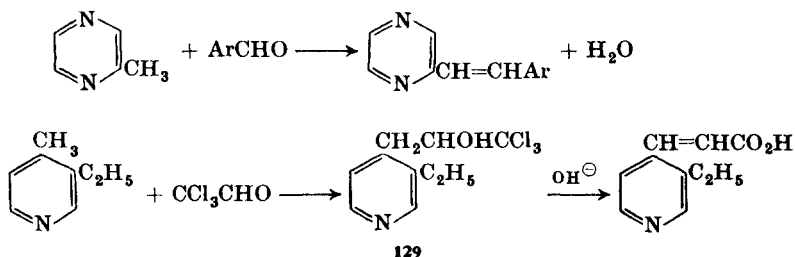
²¹⁹ Chodroff and Whitmore, *J. Am. Chem. Soc.*, **72**, 1075 (1950).

²²⁰ Balasubramanian and Baliah, *J. Chem. Soc.*, **1954**, 1845.

²²¹ Oftedahl, Baker, and Dietrich, *J. Org. Chem.*, **30**, 296 (1965).

(such as pyridine or its quaternary salts) and those in which the activation is provided by a cyclic amide system as in hydantoin or barbituric acid.

Most of the condensations using pyridines, quinolines, and related heterocycles containing a methyl group in the 2 or 4 position to the ring nitrogen atom have involved aromatic aldehydes and have led to products of the stilbazole type.²²² Generally only α - and γ -methyl groups are activated in the pyridine nucleus. Thus 4-methyl-3-ethylpyridine condenses with chloral to give **129**,²²³ but 3-ethylpyridine has been reported to be unreactive.²²⁴



The condensation with chloral (one of the few consistently successful condensations involving aliphatic aldehydes) proceeds at a temperature of 100° or below. The hydroxyl-containing products such as **129** are valuable intermediates, because on treatment with potassium hydroxide they yield the corresponding acrylic acids. As expected, quaternary compounds derived from heterocycles are more reactive in condensations,^{68, 225} as are compounds such as ethyl 2-pyridylacetate. Heterocyclic systems that have been successfully used in such condensations are pyridine,²²⁶ quinoline,²²⁷⁻²²⁹ 1,5-diazaanthracene,²³⁰ thiazole,²³¹ benzthiazole,²³² benzimidazole,²²² pyridazine,^{226, 233} quinazoline,²³⁴ quinoxaline,^{226, 234} benzoxazolone,²³⁴ pyrazine,²²⁶ pyrimidine,²²⁶ benzselenazole,²³² and

²²² Poirier, Morin, McKim, and Bearse, *J. Org. Chem.*, **28**, 4277 (1961).

²²³ Rabe, Hüntenburg, Schultze, and Volger, *Ber.*, **64**, 2493 (1931).

²²⁴ Mikhlina and Rubtsov, *J. Gen. Chem. USSR (English Transl.)*, **27**, 77 (1957) [*C.A.*, **51**, 12085 (1957)].

²²⁵ Jerchel and Heck, *Ann.*, **613**, 177 (1958).

²²⁶ Jones, Kornfeld, and McLaughlin, *J. Am. Chem. Soc.*, **72**, 3541 (1950).

²²⁷ Walker, *J. Chem. Soc.*, **1947**, 1686.

²²⁸ Woodward and Kornfeld, *J. Am. Chem. Soc.*, **70**, 2513, (1948).

²²⁹ Brown, Hammick, and Robinson, *J. Chem. Soc.*, **1950**, 783.

²³⁰ Ruggli and Brandt, *Helv. Chim. Acta*, **27**, 287, 290 (1944).

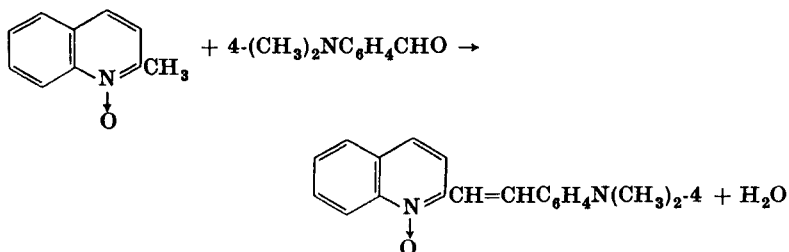
²³¹ Jones, Kornfeld, and McLaughlin, *J. Am. Chem. Soc.*, **72**, 4528 (1950).

²³² Hamer, *J. Chem. Soc.*, **1952**, 3202.

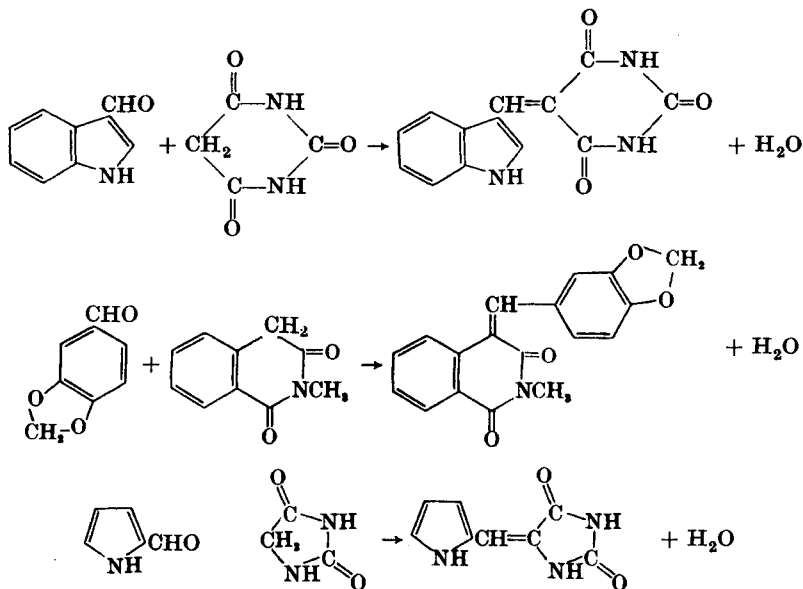
²³³ Mizzoni and Spoerri, *J. Am. Chem. Soc.*, **76**, 2202 (1954).

²³⁴ Ried and Keller, *Chem. Ber.*, **89**, 2580 (1956).

quinolizine.²³⁵ N-Oxides of pyridine and quinoline have also been condensed with aromatic aldehydes.²³⁶



The condensation of aldehydes with cyclic amides or imides is exemplified by three accompanying equations in which the methylene component is barbituric acid,²³⁷ N-methylhomophthalimide,²³⁸ and hydantoin,²³⁹ respectively. An inorganic base rather than an amine is commonly used for this kind of condensation. Other methylene components that have been used are N-methyloxindole²⁴⁰ and oxindole.²⁴¹ The alkylidene and arylidene hydantoins and thiohydantoins can be converted to the



²³⁵ Richards and Stevens, *J. Chem. Soc.*, **1958**, 3072.

²³⁶ Parker and Furst, *J. Org. Chem.*, **23**, 203 (1958).

²³⁷ Van Order and Lindwall, *J. Org. Chem.*, **10**, 132 (1945).

²³⁸ Forrest, Haworth, Pinder, and Stevens, *J. Chem. Soc.*, **1949**, 1312.

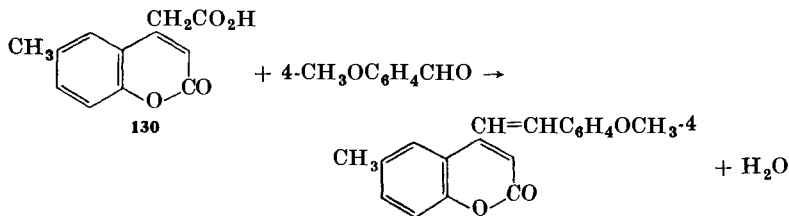
²³⁹ Harvey, *J. Chem. Soc.*, **1950**, 1638.

²⁴⁰ Freyberg and Koch, Ger. pat. 878,539 [*C.A.*, **52**, 12412 (1958)].

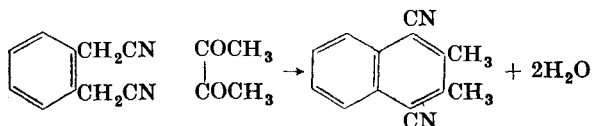
²⁴¹ Walker, *J. Am. Chem. Soc.*, **77**, 3848 (1955).

corresponding amino acids by treatment with hydriodic acid and red phosphorus.²⁴²

A number of 4-coumarinylacetic acid derivatives such as **130** condense with aromatic aldehydes forming 4-styrylcoumarin derivatives. If 4-coumarinylacetic acid is used, condensation and decarboxylation give the styrylcoumarins.^{243, 244}



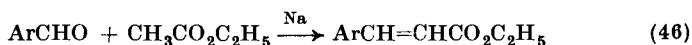
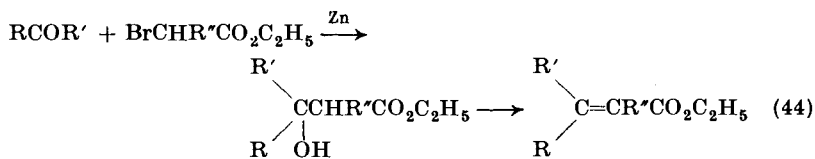
Some phenylacetonitriles have been used in condensations under the conditions of the Knoevenagel reaction, although more frequently a stronger basic catalyst is employed. Particularly interesting is the formation of aromatic rings by condensation of an *ortho* dinitrile with an α -diketone.²⁴⁵



COMPARISON WITH OTHER METHODS

The Knoevenagel condensation provides primarily a route to α,β -unsaturated acids and their derivatives and to α,β -unsaturated nitro compounds. Comparisons will be made therefore with other methods by which such compounds can be obtained.

A detailed discussion of the relative merits of the Knoevenagel synthesis of cinnamic acids with the Reformatsky (44), Perkin (45), and Claisen (46) syntheses was made in Volume I of this series.⁹⁰



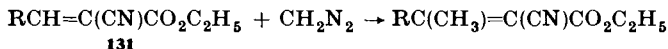
²⁴² Balenovic, Jambresic, and Furic, *J. Org. Chem.*, **17**, 1460 (1952).

²⁴³ Dey and Row, *Quart. J. Indian Chem. Soc.*, **1**, 281 (1924) [*C.A.*, **19**, 2485 (1925)].

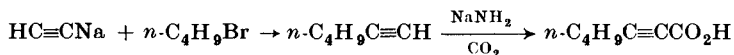
²⁴⁴ Mustafa, Kamel, and Allam, *J. Am. Chem. Soc.*, **78**, 4693 (1956).

²⁴⁵ Moureu, Chovin, and Rivoal, *Bull. Soc. Chim. France*, **1946**, 106.

The β -hydroxy esters obtained by the Reformatsky synthesis are readily dehydrated to cinnamic esters. The Knoevenagel method is far wider in scope than the Perkin and the Claisen methods and has been used successfully with practically every type of aldehyde. The Reformatsky reaction has two advantages as a general method. It can be applied to the synthesis of α -branched or β -branched cinnamic esters by using the α -bromo derivatives of higher fatty acid esters or by using ketones. The synthesis of α -alkylcinnamic acids by a modification of the Knoevenagel synthesis (p. 228) has been shown to be possible.⁶⁰ When this method fails, the cause is steric hindrance, for example when isopropylmalonic acid is used, and such hindrance should apply equally to the Reformatsky synthesis. For the direct synthesis of β -alkylcinnamic esters the Reformatsky reaction using ketones probably remains the method of choice, although the high yields obtained in condensations between cyanoacetic esters and ketones by the Cope modification of the Knoevenagel synthesis make this competitive if the cyanoacetate is readily hydrolyzed or if the Reformatsky method cannot be used, as, for example, with nitrobenzene derivatives. Recently it has been reported that cyanoacetates of the type **131** can be methylated with diazomethane to give β -methyl derivatives in good yield.²⁴⁶



A number of other methods for the synthesis of α,β -unsaturated acids and their derivatives were not described in the earlier review.⁹⁰ One of these, which is of general application and of particular usefulness in the aliphatic series, is the carboxylation of sodium acetylides or acetylenic Grignard reagents. A method has been described for the synthesis of an α,β -acetylenic acid from acetylene in a single process without isolation of the intermediate alkylacetylene.²⁴⁷ In an example, sodium acetylide is treated in liquid ammonia with *n*-butyl bromide and then with sodium. After removal of the ammonia and addition of ether or benzene, the sodium derivative is carbonated with solid carbon dioxide to give the acetylenic acid. This route has the advantage that by suitable reduction either the *cis*- or the *trans*-ethylenic acids can be obtained, whereas the

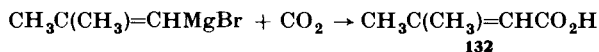


Knoevenagel synthesis gives the *trans* acid. The products of this synthesis are not branched at the α or the β position. A similar method of

²⁴⁶ Popp and Catala, *J. Org. Chem.*, **26**, 2740 (1961).

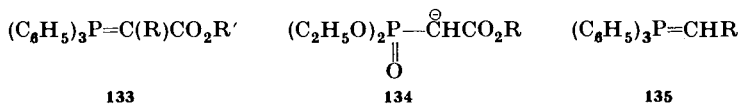
²⁴⁷ Zoss and Hennion, *J. Am. Chem. Soc.*, **63**, 1151 (1941).

synthesis which does permit branching in the β position is the carbonation of vinyl or propenyl Grignard reagents or lithium reagents. (These Grignard reagents must be prepared in tetrahydrofuran.) Thus 2-methylpropenylmagnesium bromide gives the acid **132**.²⁴⁸ The Grignard reagents are somewhat difficult to prepare because of the inertness of vinyl halides.

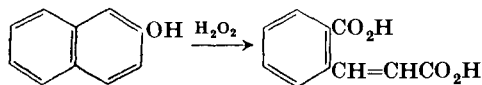


An ingenious route to α,β -unsaturated esters involves the interaction of the lithium, sodium, or Grignard reagent from ethoxyacetylene with an aldehyde or ketone. The intermediate acetylenic alcohols are unstable to acid and rearrange (often in the cold) to give α,β -unsaturated esters.²⁴⁹

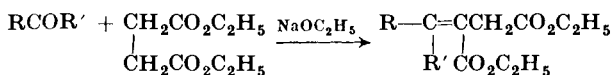
A new method, which shows much promise in the synthesis of α,β -unsaturated esters, amides, and nitriles, uses the Wittig reagent; this synthetic method is reviewed in the previous volume of this series.²⁵⁰ The usual reagent for syntheses involving aldehydes is the triphenylphosphorane, **133** ($\text{R} = \text{H}$, Br , or alkyl), but yields are much poorer with ketones and for these the anion **134** is reported to be the reagent of choice. The *trans* olefins are usually formed from the resonance-stabilized ylides **133**. A few examples of synthesis of α,β -unsaturated amides or nitriles have been reported; the ylide used here is **135** ($\text{R} = \text{CONH}_2$ or CN).



A somewhat restricted range of cinnamic acids can be obtained by the hydrogen peroxide oxidation of naphthols.²⁵¹



The rather more restricted use of the Knoevenagel synthesis with triethanolamine as catalyst to give β,γ -unsaturated esters in the aliphatic series is competitive with the Stobbe condensation where decarboxylation commonly gives a lactone.²⁵²



²⁴⁸ Normant and Maitte, *Bull. Soc. Chim. France*, **1956**, 1439.

²⁴⁹ Heilbron, Jones, Julia, and Weedon, *J. Chem. Soc.*, **1949**, 1823.

²⁵⁰ Maercker, *Org. Reactions*, **14**, 270-490 (1964).

²⁵¹ Ames and Davey, *J. Chem. Soc.*, **1958**, 1794.

²⁵² Johnson and Daub, *Org. Reactions*, **6**, 1-73 (1951).

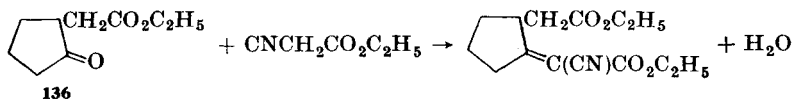
It must be emphasized that the mildness of the usual catalysts and experimental conditions for the Knoevenagel condensation make it the method of choice when sensitive groups are present in the aldehyde or ketone.

For the preparation of α,β -unsaturated acids or esters from the corresponding saturated compounds, dehydrohalogenation of α -halo acids may be mentioned. The Hell-Volhard-Zelinsky bromination of a carboxylic acid gives an α -bromo derivative, and elimination of hydrogen bromide from this is stereospecific. More easily brominated are the malonic acids or esters which are available by the standard malonic ester synthesis.

For the synthesis of α,β -unsaturated nitro compounds a basic catalyst is generally used, but this may be a strong base such as sodium hydroxide, or an organic base. It has been reported that sodium hydroxide tends to produce nitro alcohols, whereas organic bases favor nitroethylene formation.¹⁹⁸

SELECTION OF EXPERIMENTAL CONDITIONS

The choice of catalyst for the Knoevenagel synthesis of cinnamic acids has been dealt with in Chapter 8 of Volume I in this series.⁹⁰ The most generally used catalyst is still pyridine with or without added piperidine, while for the production of arylidenemalonic acids alcoholic ammonia is preferred. Piperidine or other secondary amines are suitable for the condensations which involve malonic esters, malononitrile, β -diketones, β -ketonic esters, and methyl groups activated by attachment to a heterocyclic or nitro aromatic system. A study of condensations between ketones and ethyl cyanoacetate led to the suggestion that ammonium acetate is the best catalyst for condensations with hindered ketones, and primary amines, especially benzylamine, for unhindered ketones and aldehydes.²⁵³ A startling increase in yield in condensations involving ketones carrying other functional groups (notably ester groups) was obtained by the use of piperidine containing a little benzylamine. The cyclopentanone **136** condensed with ethyl cyanoacetate to give the unsaturated compound in 55% yield with piperidine as catalyst. With added benzylamine the yield was 89%.²⁵³



Secondary amines are on the whole less successful in condensations involving aliphatic nitro compounds, where the catalyst of choice is a

²⁵³ Dev, *J. Indian Chem. Soc.*, **30**, 665 (1953).

primary amine or ammonium acetate in boiling benzene. In a comparative study the latter was found superior.²⁵⁴ The Schiff bases can be used without catalysts.

The most significant modification of the Knoevenagel reaction has been the introduction by Cope of ammonium and amine acetates as catalysts. They are used with a solvent mixture of acetic acid (minor component) and some water-immiscible solvent such as benzene, chloroform, or toluene (major component).^{46, 47} By boiling the reaction mixture and using a Dean-Stark water separator the reaction can be accelerated and the progress of the reaction observed. Modified apparatus for this type of condensation has been described by Wideqvist²⁵⁵ and by Raha.²⁵⁶ The latter author has studied the yields obtained with a variety of second solvents and has found the most effective to be benzene and toluene, followed by chloroform and hexane. The Cope modification has proved most valuable for condensations involving cyanoacetic esters, but it has been used successfully for reactions with malononitrile, malonic esters, cyanoacetamide, acetoacetic esters, alkyl- and aryl-sulfonylacetic esters, and aliphatic nitro compounds. Variations in the acid component include the use of benzoic and caproic acids to minimize the loss of amine salt by amide formation during prolonged reactions. Increase in yield by reduction in acetamide formation has also been achieved by adding the ammonium acetate catalyst at intervals during lengthy reactions.¹³⁷ In some cases, however, this has been reported to be without effect.²⁵⁶

The suggestion that amine salts are active catalysts has led to the use of amino acids.¹⁰⁶ An extensive range of amino acids has been tested and four selected as superior. All give yields of the same order as piperidinium acetate under Cope conditions in the condensation between acetone and ethyl cyanoacetate. The four selected (*p*-aminophenol, α -aminophenylacetic acid, β -alanine, and ϵ -aminocaproic acid) were used with acetic acid and benzene; it was found that with increasing amounts of *p*-aminophenol the acetic acid became unnecessary. A number of successful condensations have been performed with weakly basic resins such as Amberlite IR-4B^{181, 257} and Dowex 3,¹⁴¹ preferably in the acetate or benzoate form. The resins have the advantage of easy removal by filtration after completion of the reaction. The use of triethanolamine to obtain high yields of β,γ -unsaturated acid in the malonic acid condensation has been mentioned.⁵⁸ No general rules regarding temperature of reaction can be given, although it has been reported that a number of aromatic aldehydes

²⁵⁴ Gairaud and Lappin, *J. Org. Chem.*, **18**, 3 (1953).

²⁵⁵ Wideqvist, *Acta Chem. Scand.*, **3**, 303 (1949).

²⁵⁶ Raha, *J. Indian Chem. Soc.*, **30**, 206 (1953).

²⁵⁷ Mastagli, Lambert, and Andric, *Bull. Soc. Chim. France*, **1956**, 797.

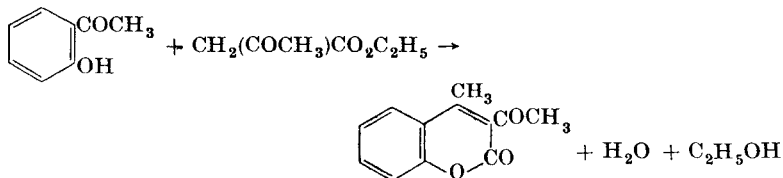
failed to condense with malonic acid at -10° to -6° .²⁵⁸ The reader is referred to the tables for details of temperature.

The proportion of catalyst used varies considerably from a large excess (as with pyridine in the Verley-Doebner modification of the cinnamic acid synthesis^{8,9}) to a few drops, as commonly with piperidine. A number of studies of individual reactions with the intention of discovering the optimum amount of catalyst have not led to any general rule. In some cases 0.1 to 0.2 mole of catalyst to each mole of aldehyde has been used; in others a 1:1 ratio; in others a large excess of catalyst.^{58, 60, 259} The usual proportion of ammonium acetate or amine acetate in the Cope modification is 0.2 mole to each mole of active methylene component. Variations in concentration of the acetic acid alter the yield in the condensation between ethyl pyruvate and ethyl cyanoacetate, the maximum yield being attained with a concentration of 0.075–0.1 *M*.²⁶⁰ In the condensation of furfural with acetylacetone in water using glycine as catalyst the yield of condensation product rose with increasing concentration of catalyst, but this may have been due in part to a salting-out effect.⁴⁰

A considerable increase in yield and in rate of reaction was achieved by application of high pressures (15,000 atmospheres) to the condensation between cyclopentanone and ethyl cyanoacetate.²⁶¹ Using cyclohexanone the condensation could be achieved without the piperidine catalyst.

Catalysts Other Than Amines or Their Salts

Catalysts other than amines or their salts have been used frequently in condensation between aldehydes or ketones and active methylene compounds. Among the more common catalysts are caustic alkalies or sodium carbonate, the latter in what amounts to an extension of the aldol condensation; and, less often, quaternary ammonium hydroxides or strongly basic resins. An example of the use of quaternary ammonium hydroxide resins is the formation of the coumarin from ethyl acetoacetate and *o*-hydroxyacetophenone.²⁶²



²⁵⁸ Das and Dutt, *Proc. Acad. Sci., Agra Oudh*, **4**, 290 (1934/5) [*C.A.*, **29**, 7946 (1935)].

²⁵⁹ Dalal and Dutt, *J. Indian Chem. Soc.*, **9**, 311 (1932).

²⁶⁰ Raha, *J. Indian Chem. Soc.*, **34**, 537 (1957).

²⁶¹ Newitt, Linstead, Sapiro, and Boorman, *J. Chem. Soc.*, **1937**, 876.

²⁶² Mastagli and Andrie, *Compt. Rend.*, **246**, 3079 (1958).

Catalysis by sodium hydroxide is as common as the use of amines in the condensation of cyanoacetic acid with aldehydes. Sodium cyanoacetate, as synthesized in aqueous alkaline solution, can be used directly in the condensation.²⁶³ Condensations involving malonic esters have been performed with acetic anhydride or zinc chloride as catalyst, and a number of cases have been recorded for which the yields were higher with acetic anhydride than with piperidinium acetate.⁴⁷ Potassium fluoride has been used extensively in recent years as a catalyst for condensations involving malonic esters,^{264, 264a} and cyanoacetic esters.²⁶⁵⁻²⁶⁸ Most of the yields reported are lower than those obtained by using conventional Knoevenagel catalysts. Titanium tetrachloride has been used to catalyze the condensation of aldehydes with ethyl malonate, ethyl acetoacetate, and ethyl cyanoacetate.²⁶⁹

EXPERIMENTAL PROCEDURES

Procedures for the preparation of cinnamic acid in 54-57% yield from benzaldehyde, malonic acid, and α -picoline;²⁵⁹ *p*-methoxycinnamic acid in 45-50% yield from 4-methoxybenzaldehyde, malonic acid, and ethanolic ammonia; β -piperonylacrylic acid in 85-90% yield from piperonal (3,4-methylenedioxybenzaldehyde), malonic acid, and pyridine with piperidine; ferulic acid in 70-85% yield from 3-methoxy-4-hydroxybenzaldehyde, malonic acid, and pyridine with piperidine;²⁷⁰ and β -*n*-hexylacrylic acid in 75-85% yield from *n*-heptaldehyde, malonic acid, and pyridine⁷³ are reported in an earlier volume of this series.⁹⁰ Procedures for the synthesis of 2,3-dimethoxycinnamic acid from 2,3-dimethoxybenzaldehyde, malonic acid, and pyridine with piperidine (in 87-98% yield)²⁷¹ and for 3-nitrocinnamic acid from 3-nitrobenzaldehyde, malonic acid, and pyridine (in 75-80% yield)²⁷² are given in detail in volumes of *Organic Syntheses*.

²⁶³ Lapworth and Baker, *Org. Syntheses*, Coll. Vol. 1, 181 (1941).

²⁶⁴ Sakurai, Midorikawa, and Aoyama, *J. Sci. Res. Inst. (Tokyo)*, **52**, 112 (1958) [*C.A.*, **53**, 15961 (1959)].

^{264a} Rand, Swisher, and Cronin, *J. Org. Chem.*, **27**, 3505 (1962).

²⁶⁵ Baba, Midorikawa, and Aoyama, *J. Sci. Res. Inst. (Tokyo)*, **52**, 99, (1958) [*C.A.*, **53**, 15960 (1959)].

²⁶⁶ Igarashi, Midorikawa, and Aoyama, *J. Sci. Res. Inst. (Tokyo)*, **52**, 105 (1958) [*C.A.*, **53**, 15960 (1959)].

²⁶⁷ Igarashi, Midorikawa, and Aoyama, *J. Sci. Res. Inst. (Tokyo)*, **52**, 151 (1958) [*C.A.*, **53**, 15961 (1959)].

²⁶⁸ Yasuda, Midorikawa, and Aoyama, *J. Sci. Res. Inst. (Tokyo)*, **53**, 19 (1959) [*C.A.*, **54**, 3192 (1960)].

²⁶⁹ Mastagli, Gnanadickam, and Lambert, *Compt. Rend.*, **254**, 1295 (1962); Gnanadickam, *Ann. Chim. (Paris)*, **7**, 807 (1962).

²⁷⁰ Vorsatz, *J. Prakt. Chem.*, **145**, 265 (1936).

²⁷¹ Koo, Fish, Walker, and Blake, *Org. Syntheses*, Coll. Vol. 4, 327 (1963).

²⁷² Wiley and Smith, *Org. Syntheses*, Coll. Vol. 4, 731 (1963).

2-Methoxycinnamic Acid.⁸⁷ 2-Methoxybenzaldehyde diethyl acetal (0.1 mole), malonic acid (0.2 mole), pyridine (42 ml.), and piperidine (2 ml.) are heated at 100° for 3 hours and at 140° for 30 minutes. The mixture is then cooled and poured onto ice and concentrated hydrochloric acid. Separation of the precipitated material and recrystallization from ethanol gives an almost quantitative yield of 2-methoxycinnamic acid, m.p. 180°.

Ethyl 3,4,5-Trimethoxycinnamate.²⁷³ To a solution of 3,4,5-trimethoxybenzaldehyde (25 g.) and ethyl hydrogen malonate (35 g.) in dry pyridine (75 ml.) are added a few drops of aniline and piperidine and some boiling stones, and the mixture is heated on a boiling water bath until no more carbon dioxide is evolved (5–8 hours). The mixture is then poured into 2*N* hydrochloric acid (1 l.). The oily precipitate crystallizes after a while and is distilled at about 180°/0.5 mm. The ester crystallizes from aqueous ethanol as colorless needles, m.p. 68° (71%).

The synthesis of *ethyl coumarin-3-carboxylate* in 78–83% yield from salicylaldehyde, diethyl malonate, and piperidine with piperidinium acetate is described in detail in *Organic Syntheses*.²⁷⁴

β -(5-Methyl-2-thienyl)- β -aminopropionic Acid.²⁷⁵ 5-Methylthiophene-2-carboxaldehyde (32.5 g.), malonic acid (30.5 g.), and ammonium acetate (49.0 g.) are mixed in 96% ethanol (100 ml.), and the solution is boiled on a water bath for 6 hours. Ammonium acetate (49.0 g.) and 96% ethanol (50 ml.) are added, and the mixture is boiled again for 6 hours. The crystals which separate are collected on a filter and washed with ethanol and diethyl ether to give the crude amino acid (10.45 g.), m.p. 205–206° (dec.). The filtrate and washings are combined and concentrated under reduced pressure to 200 ml. An additional 30.0 g. of ammonium acetate is added and the mixture boiled on a water bath for 6 hours. The ethanol and part of the ammonium acetate are removed under vacuum, and water (400 ml.) is added. The acrylic acid separates as an oil and is extracted with diethyl ether. The aqueous layer is separated and freed from ether by blowing air through it. The aqueous layer is neutralized by sodium hydroxide until just acid to litmus, and saturated aqueous cupric acetate is added, giving the copper salt of the amino acid (9.48 g.). Decomposition with hydrogen sulfide gives 5.3 g. of amino acid. The total yield of the β -amino acid is 15.7 g. (33%). After recrystallization from water the acid melts at 208°.

The preparation of *ethyl 2-cyano-3-ethyl-2-pentenoate* (in 60–68% yield)

²⁷³ Freudenberg and Schraube, *Chem. Ber.*, **88**, 22 (1955).

²⁷⁴ Horning, Horning, and Dimmig, *Org. Syntheses*, Coll. Vol. **3**, 165 (1955).

²⁷⁵ Gol'dfarb, Fabrichnyi, and Shalavina, *J. Gen. Chem. USSR (English Transl.)*, **28**, 213 (1958) [*C.A.*, **52**, 12838 (1958)].

from diethyl ketone, ethyl cyanoacetate, ammonium acetate, and acetic acid in benzene (Cope conditions) is given in detail in *Organic Syntheses*.²⁷⁶

The reductive condensation of *n*-butyraldehyde with ethyl cyanoacetate to give *ethyl n-butylcyanoacetate* in 94–96% yield using piperidinium acetate and a palladium catalyst is described in detail in *Organic Syntheses*.²⁷⁷

Ethyl Cyclohexylidenecyanoacetate.¹⁴¹ Cyclohexanone (20.7 ml.), ethyl cyanoacetate (21.3 ml.), Dowex 3 acetate (5 g., formed *in situ* from equimolar amounts of the resin and acetic acid), and benzene (75 ml.) are boiled under reflux, the water formed being separated with a Dean-Stark trap. After 6 hours the mixture is cooled, filtered, and distilled under vacuum giving ethyl cyclohexylidenecyanoacetate, b.p. 98–99°/0.10–0.12 mm., n_D^{25} 1.4939. The yield is quantitative.

Ethyl α -Cyano- β -methyl-2-pentenoate.¹⁰⁶ Methyl ethyl ketone (346 g.) and ethyl cyanoacetate (453 g.) in benzene (400 ml.) are boiled with ϵ -aminocaproic acid (2.6 g.) and acetic acid (80 gm.) for 7 hours. Progress of the condensation is observed by separation of the water in a Barret trap. After removal of the benzene, the residue is distilled at 115–120°/12 mm, giving ethyl α -cyano- β -methyl-2-pentenoate, n_D^{25} 1.4638–1.4649. The yield is 533 g. (80%).

The synthesis of *cyclohexylidenecyanoacetic acid* in 65–76% yield from cyclohexanone, cyanoacetic acid, and ammonium acetate in benzene is described in detail in *Organic Syntheses*.¹²⁷ Also described is the decarboxylation of the crude cyanoacetic acid to give *cyclohexylideneacetone nitrile* in 76–91% yield.

α -Cyano- β -4-di-(2'-chloroethyl)aminophenylacrylic Acid.²⁷⁸ To a mixture of 4-[N,N-di-(2'-chloroethyl)amino]benzaldehyde (2.46 g., 0.01 mole) and cyanoacetic acid (0.85 g., 0.01 mole) in dry dioxane (15–25 ml.) at 0°, piperidine (~0.2 ml.) is added dropwise. The mixture is kept overnight at room temperature, and crystals form. The α -cyano- β -[4-di-(2'-chloroethyl)amino]phenylacrylic acid is recrystallized from chloroform, m.p. 206–207° (97%).

The synthesis of 3-(2'-furyl)acrylonitrile from furfural, cyanoacetic acid, and ammonium acetate in 74–78% yield is described in detail in *Organic Syntheses*.¹²⁹

4-Chlorocinnamonitrile.⁶⁷ 4-Chlorobenzaldehyde (14.06 g.) and cyanoacetic acid (8.9 g., technical grade) in pyridine (50 ml.) and piperidine (1 ml.) are heated to boiling (bath temperature 135–140°) for 5 hours. The major part of the base is removed under reduced pressure, and the

²⁷⁶ Cope and Hancock, *Org. Syntheses*, Coll. Vol. **3**, 399 (1955).

²⁷⁷ Alexander and Cope, *Org. Syntheses*, Coll. Vol. **3**, 385 (1955).

²⁷⁸ Popp, *J. Chem. Soc.*, **1960**, 5271.

oily residue is dissolved in benzene. The benzene solution is shaken with aqueous sodium bisulfite, giving the bisulfite compound of unchanged 4-chlorobenzaldehyde (1.78 g.). The filtrate is washed with water, sodium carbonate solution, and again with water. The benzene is removed and the crude residue crystallized from petroleum ether, giving 4-chlorocinnamionitrile, m.p. 84–87° (11.7 g., 72%). The nitrile distills unchanged at 1 mm., leaving a residue which distills at 165–172°/0.1 mm. (2 g.) and which, on boiling for 6 hours with an equal weight of potassium hydroxide in three parts of water, furnishes β -(4'-chlorophenyl)glutaric acid, m.p. 162–165°.

β -(3,4-Methylenedioxyphenyl)glutaronitrile.¹³³ 3,4-Methylenedioxybenzaldehyde (7.5 g.) and cyanoacetic acid (10.46 g.) in pyridine (30 ml.) with piperidine (1 ml.) are heated to boiling for 5.5 hours. The major proportion of the base is removed under vacuum and the oily residue dissolved in benzene. The benzene solution is washed with bisulfite solution, water, sodium carbonate solution, and again with water. After removal of benzene under vacuum, the residual oil is purified by crystallization from a benzene-petroleum ether mixture, giving β -(3,4-methylenedioxyphenyl)glutaronitrile, m.p. 69–71° (84%).

The synthesis of 3-methylglutaric acid in 80% yield from acetaldehyde, cyanoacetamide, and piperidine via the intermediate bis-cyanoacetamide condensation product is described in detail in *Organic Syntheses*.²⁷⁹

1-Dicyanomethylene-2-phenylcyclohexane.²⁸⁰ 2-Phenylcyclohexanone (86.6 g.), malononitrile (33.0 g.), ammonium acetate (7.7 gm.), acetic acid (4.6 ml.), and benzene (100 ml.) are stirred and boiled for 12 hours under reflux using a Dean-Stark water separator. The solution is washed with water, then with 1M sodium carbonate, and evaporated. The residue is crystallized from ethanol to give the dicyanomethylene derivative, m.p. 67–68°. The yield is 107.6 g. (97%).

Piperonylidene malononitrile.¹⁰⁵ To a solution of piperonal (3,4-methylenedioxybenzaldehyde) (30 g., 0.2 mole) and malononitrile (15 g., 0.24 mole) in *n*-butyl alcohol (130 ml.), 8 drops of piperidine is added, with stirring. Within 5 minutes the mixture becomes solid. After it is cooled to room temperature the product is filtered by suction, washed with water containing a little acetic acid, and air dried. The yield of nitrile is 38 g. (96%). A sample, recrystallized from acetic acid and dried at 100°, melts at 199–200°.

1-Acetyl-1-carbethoxy-3,4,5,6-diisopropylidene-D-arabohexos-1-ene.¹⁷⁴ A solution of 3,4,5,6-diisopropylidene-D-arabinose (2.3 g.) and ethyl acetoacetate (1.33 g.) with 3 drops of diethylamine in 50 ml. of

²⁷⁹ Kent and McElvain, *Org. Syntheses*, Coll. Vol. 3, 591 (1955).

²⁸⁰ Murphy, *J. Org. Chem.*, 28, 3107 (1961).

toluene is kept at 0° for 7 days, during which time some water separates. Toluene is removed under vacuum at 40° bath temperature, and the residual syrup is distilled at 105–115° (bath temperature) and 5×10^{-4} mm. pressure. The yield is 2.53 g. (75%) of a yellow oil, n_D^{20} 1.4640, $[\alpha]_D^{19} + 24.2^\circ$ ($c = 2.92$, in methanol).

Ethyl *n*-Butylideneacetoacetate.¹⁸² A mixture of ethyl acetoacetate (65 g., 0.5 mole) and freshly distilled *n*-butyraldehyde (36 g., 0.55 mole) is cooled to -5°. Piperidine (0.5 g.) in 1 g. of ethanol is added during 5–10 minutes so that the temperature does not rise above +5° to +10°. The mixture is cooled to 0° and placed in a refrigerator for 12–24 hours after which the ester is washed with three 100-ml. portions of water containing a few drops of acetic acid. The washings are extracted with diethyl ether, and the combined ether extracts and ester layer are distilled through a Widmer column. The yield of ethyl *n*-butylideneacetoacetate, b.p. 118–120°/18 mm., n_D^{25} 1.4510, d_{25} 0.9780, Mol. refr. 50.81, is 71.4 g. (81%).

Ethyl 2,5-Dimethylthienylidene-*bis*-acetoacetate and β -2,5-Dimethylthienylglutaric Acid.¹⁸³ (a) 2,5-Dimethyl-3-thiophenecarboxaldehyde (14.0 g., 0.10 mole) and ethyl acetoacetate (26.0 g., 0.20 mole) are mixed and 1.0 ml. of piperidine added. After 36 hours at room temperature the cloudy mixture is placed in a refrigerator for several hours, after which scratching with a glass rod produces a solid mass of crystals. The cake is broken up, pressed on a Büchner funnel, dissolved in 20 ml. of warm ethanol, and, after several hours, the solid is filtered and washed with 5 ml. of ethanol. The product (26.1 g., 68%) is sufficiently pure for stage (b), but a sample can be recrystallized from a 1:2 benzene-ligroin mixture to give pure ethyl 2,5-dimethylthienylidene-*bis*-acetoacetate, m.p. 116–117°.

(b) The ethyl *bis*-acetoacetate (7.0 g.) is dissolved in 50 ml. of ethanol, and 50 ml. of a solution of 50 g. of sodium hydroxide in 50 ml. of water is added. The mixture is boiled for 1 hour, transferred to a beaker with 200 ml. of water, and 40 ml. of ethanol is removed by distillation. Then 45 ml. of water is added, and the mixture is cooled in ice. Concentrated hydrochloric acid (100 ml.) is added (the temperature being kept below 50°) and then another small quantity of acid until the mixture is acid to Congo red paper. The precipitated glutaric acid is filtered and recrystallized from water, m.p. 148–149° (62%).

6-Bromo-3-acetylcoumarin.²⁸¹ To a mixture of 5-bromosalicylaldehyde (2 g.) and ethyl acetoacetate (1.5 g.) which has been warmed gently to render it homogeneous, 3 or 4 drops of pure piperidine is added,

²⁸¹ Buu Hoi, Loc, and Xuong, *Bull. Soc. Chim. France*, **1957**, 562.

and the mixture is kept in a well-stoppered flask for 24 hours. Trituration with alcohol gives a solid which crystallizes from benzene as colorless needles, m.p. 223°. The yield is 2.1 g. (78%).

The synthesis of *ethyl 3,5-dimethyl-5-cyclohexenone-4-carboxylate* in 45–50% yield from acetaldehyde, ethyl acetoacetate, and piperidine, via the intermediate *bis*-acetoacetate, is described in detail in *Organic Syntheses*.²⁸²

3,5-Diacetyl-4-(4'-dimethylaminophenyl)heptane-2,6-dione.¹⁷¹ Acetylacetone (10 g., 0.1 mole) and 4-dimethylaminobenzaldehyde (7.5 g., 0.05 mole) are dissolved in 95% ethanol (60 ml.). About 10 drops of piperidine is added, and the mixture is allowed to stand at room temperature for 3 days until the *bis*-(β -diketone) crystallizes. The product (7.5 g.) is filtered and crystallized from benzene. It melts at 187–189°.

Propionaldehyde Methone Derivative.¹⁶⁹ Propionaldehyde (100 mg.) and methone (dimedone) (400 mg.) are dissolved in 4 ml. of 50% ethanol. One drop of piperidine is added, and the mixture is heated under reflux for 5 minutes. Water is added until the solution is slightly cloudy, and the mixture is cooled. Filtration and recrystallization from aqueous methanol gives the methone derivative of propionaldehyde, m.p. 157–158°.

α -Nitro-4-dimethylaminostyrene.²⁸³ A mixture of 4-dimethylaminobenzaldehyde (14.9 g., 0.1 mole) and nitromethane (18.3 g., 0.3 mole) is heated on a water bath until a dark green solution results. *n*-Amylamine (0.43 g.) is added and, after 20 minutes, a red crystalline mass is obtained. The mixture is allowed to stand overnight and is then filtered. Recrystallization from 2-nitropropane gives α -nitro-4-dimethylaminostyrene, m.p. 179–180.5° (16 g., 83%).

4-Chloro- α' -nitrostilbene.²⁸ A solution of 4-chlorobenzaldehyde (14.05 g., 0.1 mole) and *n*-butylamine (7.3 g., 0.1 mole) in 25–30 ml. benzene is heated under reflux in a flask fitted with a water separator until no more water is formed (15–30 minutes). Removal of the benzene gives the crude Schiff base. A solution of phenylnitromethane (13.7 g., 0.1 mole) in acetic acid is mixed with the crude Schiff base, and the mixture is allowed to stand at room temperature until crystallization is complete (2–7 hours). The solid is filtered, washed with water, and crystallized from ethanol to give 4-chloro- α' -nitrostilbene, m.p. 113–114° (75%).

3-Methyl-2-(3',3',3'-trichloro-2'-hydroxypropyl)quinoline.²²⁹ A mixture of 2,3-dimethylquinoline (6.0 g.), chloral (6.0 g.), and pyridine

²⁸² Horning, Denekas, and Field, *Org. Syntheses*, Coll. Vol. 3, 317 (1955).

²⁸³ Worrall and Cohen, *J. Am. Chem. Soc.*, **66**, 842 (1944).

(6.0 ml.) is heated on a steam bath for 2 hours. The solid obtained by addition of the mixture to water is washed free from pyridine and recrystallized several times from 75% aqueous ethanol, yielding 3-methyl-2-(3',3',3'-trichloro-2'-hydroxypropyl)quinoline (9.0 g., 75%) as colorless needles, m.p. 134–135°.

Stilbazole Methiodide.²⁸⁴ A mixture of benzaldehyde (0.03 mole) and 2-picoline methiodide (0.021 mole) in methanol (25–30 ml.) is heated for 1 to 4 hours on a water bath. After the reaction mixture has cooled, the stilbazole methiodide is filtered and recrystallized from methanol, m.p. 230–231°, λ_{\max} 3340 Å (in H₂O). The yield is 73% (6.76 g.).

TABULAR SURVEY

Each of the twenty tables that follows represents the condensations performed with a particular active methylene compound, such as malonic acid, or with a group of related active methylene compounds such as β -ketonic esters. Each table is subdivided into as many as necessary of the following five classes of aldehydes and ketones: (A) acyclic aldehydes or ketones; (B) alicyclic aldehydes or ketones; (C) aralkyl aldehydes or ketones; (D) aromatic aldehydes or ketones; (E) heterocyclic aldehydes or ketones.

Generally speaking, an aldehyde or ketone will appear in the lowest letter division to which it can be assigned. For example, any aldehyde containing a heterocyclic ring will appear in group E; but only aldehydes in which the aldehyde group is directly attached to the aromatic ring will appear in group D; ketones which appear in group D will have two aryl groups attached to the carbonyl group. All other aldehydes or ketones which possess an aromatic ring system will appear in group C.

Within any group the aldehydes and ketones are arranged in order of increasing number of carbon atoms, subdivided in order of increasing number of hydrogen atoms, and for any mixture of isomers the aldehydes appear before the ketones. Where a number of different catalysts, or conditions of reaction, have been used for the same compound, these are largely listed in chronological order.



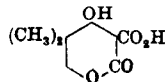
Where there is more than one reference, the one in italics is that in which the yield given was reported.

The attempt has been made to include all the examples in the literature through *Chemical Abstracts* for July 1964, but because of the nature of the reaction some omissions are inevitable.

²⁸⁴ Phillips, *J. Org. Chem.*, **12**, 333 (1947).

TABLE I
CONDENSATIONS WITH MALONIC ACID

A. Acyclic Aldehydes or Ketones

Aldehyde or Ketone	Catalyst	Temperature	Product(s) and Yield(s) (%)	Refs.
Glyoxal	Pyridine	Water bath	$\text{HO}_2\text{C}(\text{CH}=\text{CH})_2\text{CO}_2\text{H}$ (2)	12
Glyoxylic acid	"	"	Fumaric acid (10)	10, 285
Acetaldehyde	"	Boiling $\text{C}_2\text{H}_5\text{OH}$	$\text{CH}_3\text{CH}=\text{CHCO}_2\text{H}$ (54)	286
	"	Cold; dark	$\text{CH}_3\text{CH}=\text{CHCO}_2\text{H}$ (60)	287
	Piperidine + pyridine	B.p.	$\text{CH}_3\text{CH}=\text{CHCO}_2\text{H}$ (75)	285
	"	-5° to 0°	$\text{CH}_3\text{CH}=\text{C}(\text{CO}_2\text{H})_2^a$ (—)	288
	$(\text{HOCH}_2\text{CH}_2)_3\text{N}$	Room, then 100°	$\text{CH}_2=\text{CHCH}_2\text{CO}_2\text{H}^b$ (Small)	289
	$\text{NH}_3/\text{C}_2\text{H}_5\text{OH}$	B.p.	$\text{CH}_3\text{CH}(\text{NH}_3)\text{CH}_2\text{CO}_2\text{H}$ (23)	290
(Paraldehyde)	Quinoline	85°	$\text{CH}_3\text{CH}=\text{CHCO}_2\text{H}$ (40)	259
$\text{CH}_3\text{CH}(\text{OC}_2\text{H}_5)_2$	Piperidine + pyridine	B.p.	$\text{CH}_3\text{CH}=\text{CHCO}_2\text{H}$ (20)	87
Chloral	Pyridine	85°	$\text{CCl}_3\text{CH}=\text{CHCO}_2\text{H}$ (28)	291
	Piperidinium acetate	20° , then 100°	$\text{CCl}_3\text{CHOHCH}_2\text{CO}_2\text{H}$ (77)	292
CF_3CHO	Piperidine + pyridine	B.p.	$\text{CF}_3\text{CHOHCH}_2\text{CO}_2\text{H}$ (70)	35
Acrolein	Pyridine	Water bath or $35-40^\circ$	$\text{CH}_2=\text{CHCH}=\text{CHCO}_2\text{H}$ (30)	11, 293
	"	$75-80^\circ$	$\text{CH}_2=\text{CHCH}=\text{CHCO}_2\text{H}$ (50)	294
Propionaldehyde	"	Room, then 50° or water bath	$\text{C}_2\text{H}_5\text{CH}=\text{CHCO}_2\text{H}$ (50-60)	287, 295, 296
	Piperidine + pyridine	Steam bath	$\text{CH}_3\text{CH}=\text{CHCH}_2\text{CO}_2\text{H}$	
	"	Room	$\text{C}_2\text{H}_5\text{CH}=\text{CHCO}_2\text{H}$ (—)	297
	Quinoline	85°	$\text{C}_2\text{H}_5\text{CH}=\text{CHCO}_2\text{H}$ (85)	298
	$(\text{HOCH}_2\text{CH}_2)_3\text{N}$	Room, then 100°	$\text{C}_2\text{H}_5\text{CH}=\text{CHCO}_2\text{H}$ (77)	259
			$\text{CH}_3\text{CH}=\text{CHCH}_2\text{CO}_2\text{H}$ (36)	58, 289, 299
			$\text{C}_2\text{H}_5\text{CH}(\text{CH}_2\text{CO}_2\text{H})_2$ (—)	
Acetone	Ammonium malonate	Water bath	$(\text{CH}_3)_2\text{C}=\text{CHCO}_2\text{H}$ (—)	122
	Piperidine + pyridine	B.p.	$(\text{CH}_3)_2\text{C}=\text{CHCO}_2\text{H}$ (60)	285
CH_3COCF_3	"	Room, or b.p.	$\text{CF}_3\text{C}(\text{CH}_3)(\text{OH})\text{CH}_2\text{CO}_2\text{H}$ (75)	34, 35
$\text{CF}_3\text{ClCOCF}_3\text{Cl}$	"	B.p.	$(\text{CF}_3\text{Cl})_2\text{C}(\text{OH})\text{CH}_2\text{CO}_2\text{H}$ (69)	35
$n\text{-C}_4\text{F}_7\text{CHO}$	Pyridine	Boiling $\text{C}_6\text{H}_5\text{CH}_3$	$n\text{-C}_4\text{F}_7\text{CHOHCH}_2\text{CO}_2\text{H}$ (88)	36
2,2,3-Trichlorobutyraldehyde hydrate	"	Water bath	$\text{CH}_3\text{CHClCCl}_2\text{CHOHCH}_2\text{CO}_2\text{H}$ (—)	33
Crotonaldehyde	"	Steam bath or b.p.	$\text{CH}_3\text{CH}=\text{CHCH}=\text{CHCO}_2\text{H}$ (30-40)	9, 184, 300
	"	Room	$\text{CH}_3\text{CH}=\text{CHCH}=\text{C}(\text{CO}_2\text{H})_2$ (Small)	301
			$\text{CH}_3\text{CH}=\text{CHCH}=\text{CHCO}_2\text{H}$	
Crotonaldehyde diethyl acetal	Piperidine + pyridine	100° , then b.p.	$\text{CH}_3\text{CH}=\text{CHCH}=\text{CHCO}_2\text{H}$ (20)	87
2-Methylacrolein	"	Ice, then $50-55^\circ$	$\text{CH}_2=\text{C}(\text{CH}_3)\text{CH}=\text{CHCO}_2\text{H}$ (50)	302
n -Butyraldehyde	"	Steam bath	$n\text{-C}_4\text{H}_9\text{CH}=\text{CHCO}_2\text{H}$ (60)	297
	$(\text{HOCH}_2\text{CH}_2)_3\text{N}$	Room, then 100°	$\text{C}_2\text{H}_5\text{CH}=\text{CHCH}_2\text{CO}_2\text{H}$ (40)	58, 289
			$n\text{-C}_4\text{H}_9\text{CH}(\text{CH}_2\text{CO}_2\text{H})_2^d$ (—)	
Isobutyraldehyde	Piperidine + pyridine	Steam bath	$(\text{CH}_3)_2\text{CHCH}=\text{CHCO}_2\text{H}$ (66)	297
	Quinoline	85°	$(\text{CH}_3)_2\text{CHCH}=\text{CHCO}_2\text{H}$ (38)	259
$\text{CH}_3\text{CHOHCH}_2\text{CHO}$ (aldol)	Pyridine	Water bath	$\text{CH}_3\text{CH}=\text{CHCHOHCH}_2\text{CO}_2\text{H}$ (—)	301
2,3-Dihydropyran (reacting as 5-hydroxypentanal)	Piperidine + pyridine	Room, then steam bath	$\text{HOCH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}=\text{CHCO}_2\text{H}$ (30)	303
			 $\text{CH}_2\text{CO}_2\text{H}$ (6)	
3-Carbomethoxypropionaldehyde	"	Water bath, then b.p.	$\text{CH}_3\text{O}_2\text{CCH}_2\text{CH}_2\text{CH}=\text{CHCO}_2\text{H}$ (50)	304
Valeraldehyde	Piperidine or $\text{C}_2\text{H}_5\text{NH}_2\text{Cl}$	Water bath	$n\text{-C}_4\text{H}_9\text{CH}=\text{CHCO}_2\text{H}$ (—)	120, 305
	$(\text{HOCH}_2\text{CH}_2)_3\text{N}$	"	$n\text{-C}_4\text{H}_9\text{CH}=\text{CHCH}_2\text{CO}_2\text{H}$ (trans) (18)	299
Isovaleraldehyde	Pyridine	Room	$(\text{CH}_3)_2\text{CHCH}_2\text{CH}=\text{CHCO}_2\text{H}$ (—)	287
	Quinoline	85°	$(\text{CH}_3)_2\text{CHCH}_2\text{CH}=\text{CHCO}_2\text{H}$ (40)	259
	$(\text{HOCH}_2\text{CH}_2)_3\text{N}$	Room, then 100°	$(\text{CH}_3)_2\text{CHCH}_2\text{CH}=\text{CHCH}_2\text{CO}_2\text{H}$ (—)	58
Diethyl ketone	Piperidine + pyridine	B.p.	$(\text{C}_2\text{H}_5)_2\text{C}=\text{CHCO}_2\text{H}$ (35)	285
$\text{HOCH}_2\text{C}(\text{CH}_3)_2\text{CHO}$	$\text{NH}_3/\text{C}_2\text{H}_5\text{OH}$	Water bath	 +  (—)	79

Note: References 285 to 1153 are on pp. 582-599.

^a This product has been reported to be $\text{CH}_3\text{CH}(\text{CH}_2\text{CO}_2\text{H})_2$.⁵⁸

^b Some $\text{CH}_2\text{CH}(\text{CH}_2\text{CO}_2\text{H})_2$ was also formed.

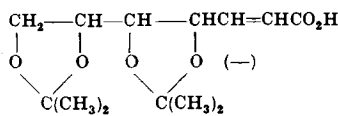
^c The acrolein was added dropwise in three portions.

^d Some of the glutaric anhydride was isolated also.

TABLE I—Continued
CONDENSATIONS WITH MALONIC ACID

276

ORGANIC REACTIONS

A. Acyclic Aldehydes or Ketones—Continued				
Aldehyde or Ketone	Catalyst	Temperature	Product(s) and Yield(s) (%)	Refs.
2-Hydroxytetrahydropyran (reacting as 5-hydroxypentanal)	Piperidine + pyridine	Room, then steam bath	$\text{HOCH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}=\text{CHCO}_2\text{H}$ (43)	303
2-Methyl-2-pentenal	Pyridine	Water bath	$\text{C}_2\text{H}_5\text{CH}=\text{C}(\text{CH}_3)\text{CH}=\text{CHCO}_2\text{H}$ (—)	11
2-Carboethoxypropionaldehyde	"	"	$\text{CH}_3\text{C}(\text{CO}_2\text{C}_2\text{H}_5)=\text{CHCH}_2\text{CO}_2\text{H}$ (40)	132
Paraldehyde (see under Acetaldehyde)	"	"	$\text{CH}_3\text{CH}(\text{CH}_2\text{CO}_2\text{H})\text{CH}=\text{CHCO}_2\text{H}^a$ (—)	306
2-Carboethoxymethylpropionaldehyde	Piperidine	Heat	$n\text{-C}_6\text{H}_{13}\text{CH}=\text{CHCO}_2\text{H}$ (—)	120
Heptanal	Pyridine	Room, then heat	$n\text{-C}_6\text{H}_{13}\text{CH}=\text{CHCO}_2\text{H}$ (86)	73, 307–309
	$\text{NH}_3/\text{C}_2\text{H}_5\text{OH}$	—	$n\text{-C}_6\text{H}_{13}\text{CH}=\text{CHCO}_2\text{H}$ (30)	310
	"	"	$n\text{-C}_6\text{H}_{13}\text{CH}(\text{NH}_2)\text{CH}_2\text{CO}_2\text{H}$ (37)	
$(n\text{-C}_3\text{F}_7)_2\text{CO}$	Piperidine + pyridine	B.p.	$(n\text{-C}_3\text{F}_7)_2\text{COHCH}_2\text{CO}_2\text{H}$ (61)	35
$n\text{-C}_7\text{F}_{15}\text{CHO}$	Pyridine	Boiling $\text{C}_6\text{H}_5\text{CH}_3$	$n\text{-C}_7\text{F}_{15}\text{CHOHCH}_2\text{CO}_2\text{H}$ (68)	36
7-Octynal	Piperidine in pyridine	50°, then room (dark)	$\text{CH}\equiv\text{C}(\text{CH}_2)_5\text{CH}=\text{CHCO}_2\text{H}$ (<i>trans</i>) (65)	311
Oct-6-en-4-ynal (<i>cis</i>)	Pyridine	20°, then 100°	$\text{CH}_3\text{CH}=\text{CHC}\equiv\text{CCH}_2\text{CH}_2\text{-CH}=\text{CHCO}_2\text{H}$ (<i>cis; trans</i>) (86) ^f	312
Oct-6-en-4-ynal (<i>trans</i>)	"	20°, then 100°	$\text{CH}_3\text{CH}=\text{CHC}\equiv\text{CCH}_2\text{CH}_2\text{-CH}=\text{CHCO}_2\text{H}$ (<i>trans; trans</i>) (34)	312
4-Octenal	"	115°	$n\text{-C}_7\text{H}_{13}\text{CH}=\text{CHCH}_2\text{CH}_2\text{CH}=\text{CHCO}_2\text{H}$ (17)	313
7-Ketooctanal	Piperidine + pyridine	0°, then 50°	$\text{CH}_3\text{CO}(\text{CH}_2)_5\text{CH}=\text{CHCO}_2\text{H}$ (<i>trans</i>) (45)	314, 315
Octanal	Pyridine	Room, then steam bath	$n\text{-C}_7\text{H}_{15}\text{CH}=\text{CHCO}_2\text{H}$ (75)	73, 308, 316
8-Hydroxyoctanal	Piperidine + pyridine	Room, then water bath	$\text{HO}(\text{CH}_2)_7\text{CH}=\text{CHCO}_2\text{H}$ (<i>trans</i>) (—)	311
2,6-Dimethylheptanal	$(\text{HOCH}_2\text{CH}_2)_3\text{N}$ or pyridine	Water bath	$(\text{CH}_3)_2\text{CH}(\text{CH}_2)_3\text{CH}(\text{CH}_3)\text{-CH}=\text{CHCO}_2\text{H}$ (29)	317
	"	"	$(\text{CH}_3)_2\text{CH}(\text{CH}_2)_3\text{C}(\text{CH}_3)=\text{CH-CH}_2\text{CO}_2\text{H}$ (75)	
Nonanal	Pyridine	Room, then water bath	$n\text{-C}_8\text{H}_{17}\text{CH}=\text{CHCO}_2\text{H}$ (46)	308
9-Hydroxynonanal	Piperidine + pyridine	Room, then steam bath	$\text{HO}(\text{CH}_2)_8\text{CH}=\text{CHCO}_2\text{H}^g$ (<i>trans</i>) (40)	311
4-Phenoxybutyraldehyde	"	"	$\text{C}_6\text{H}_5\text{OCH}_2\text{CH}_2\text{CH}_2\text{CH}=\text{CHCO}_2\text{H}$ (30–35)	318
Citral				
	Pyridine	110–120°	Citrylideneacetic acid (30)	8
	Piperidine	Heat	Citrylideneacetic acid ^b (25)	120
	Quinoline	85°	Citrylideneacetic acid ^b (95)	259
6-Decenal (<i>trans</i>)	Pyridine	Room, then steam bath	Citrylideneacetic acid (74)	316
	"	"	<i>trans, trans</i> - $n\text{-C}_3\text{H}_7\text{CH}=\text{CH}(\text{CH}_2)_4\text{-CH}=\text{CHCO}_2\text{H}$ (45)	
Citronellal	"	70°, or water bath	$(\text{CH}_3)_2\text{C}=\text{CHCH}_2\text{CH}_2\text{CH}(\text{CH}_3)\text{-CH}_2\text{CH}=\text{CHCO}_2\text{H}$ (75–90)	317, 319, 320
	Quinoline	85°	"Citronellylideneacetic acid" (37)	259
8-Acetoxyoctanal	Piperidine + pyridine	50° (dark)	$\text{CH}_3\text{CO}_2(\text{CH}_2)_7\text{CH}=\text{CHCO}_2\text{H}$ (<i>trans</i>) (73)	62
Decanal	" or pyridine	Room, then water bath	$n\text{-C}_9\text{H}_{19}\text{CH}=\text{CHCO}_2\text{H}$ (58)	73, 308
3-Methylnonanal	Piperidine + pyridine	60°, then boil	$n\text{-C}_8\text{H}_{17}\text{CH}(\text{CH}_3)\text{CH}_2\text{CH}=\text{CHCO}_2\text{H}$ (Small)	322
$(\text{CH}_3)_2\text{CH}(\text{CH}_2)_3\text{CH}(\text{CH}_3)\text{CH}_2\text{CHO}$	"	100°	$(\text{CH}_3)_2\text{CH}(\text{CH}_2)_3\text{CH}(\text{CH}_3)\text{-CH}_2\text{CH}=\text{CHCO}_2\text{H}$ (—)	323
10-Hydroxydecanal	"	Room, then water bath	$\text{HO}(\text{CH}_2)_9\text{CH}=\text{CHCO}_2\text{H}$ (—)	311
2,3,4,5-Diisopropylidenearabinose (aldehyde)	"	100°	$\text{CH}_2\text{-CH-CH-CHCH}=\text{CHCO}_2\text{H}$ 	324
8-Carboethoxyoctanal	Pyridine	Room, then steam bath	$\text{HO}_2\text{C}(\text{CH}_2)_7\text{CH}=\text{CHCO}_2\text{H}^i$ (30–50)	325

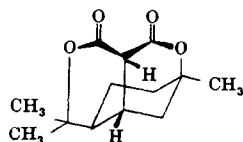
Note: References 285 to 1153 are on pp. 582–599.

^a The crude ester was hydrolyzed

^f The yield given is of crude product.

^g This yield was based on the preparation and immediate condensation of the hydroxy aldehyde.

^b This compound was shown to be







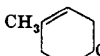

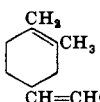

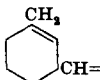

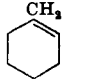
. See ref. 321.

ⁱ The crude product was hydrolyzed.

277

THE KNOEVENAGEL CONDENSATION

TABLE I—Continued
CONDENSATIONS WITH MALONIC ACID


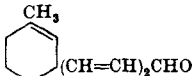
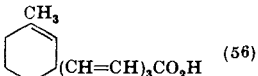
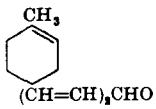
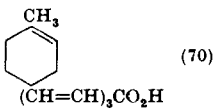
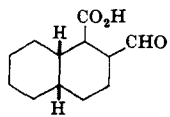
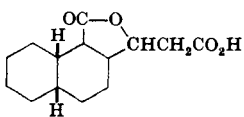
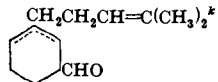
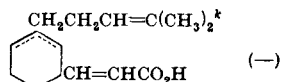
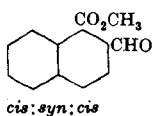
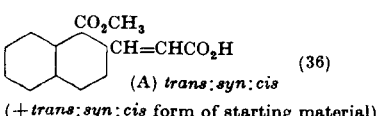
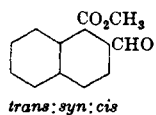
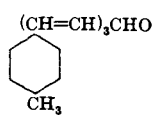
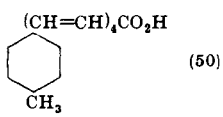
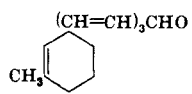
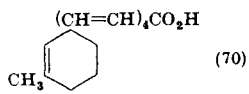
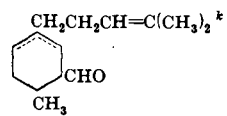
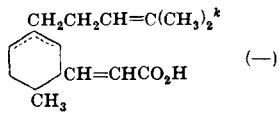
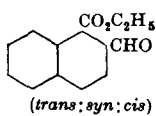
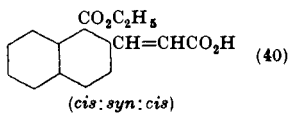
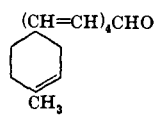
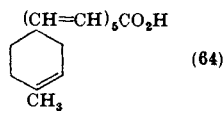
A. Acyclic Aldehydes or Ketones—Continued				
Aldehyde or Ketone	Catalyst	Temperature	Product(s) and Yield(s) (%)	Refs.
8-Carbethoxyoctanal (<i>contd.</i>)	$C_6H_5N(CH_3)_2$	Room, then	$HO_2C(CH_2)_6CH=CHCH_2CO_2H^†$ (—)	325
9-Carbomethoxynonanal	Pyridine	steam bath	$HO_2C(CH_2)_7CH=CHCO_2H^†$ (30–50)	325
	$C_6H_5N(CH_3)_2$	"	$HO_2C(CH_2)_7CH=CHCH_2CO_2H^†$ (—)	325
Undecanal	Pyridine or piperidine + pyridine	Room, then water bath	$n-C_{10}H_{21}CH=CHCO_2H$ (67)	73, 308
$CH_3(CH=CH)_5CHO$	Piperidine + pyridine	Water bath	$CH_3(CH=CH)_5CO_2H$ (65)	326
10-Acetoxydecanal	"	50–55°, then 90°	$CH_3CO_2(CH_2)_8CH=CHCO_2H$ (<i>trans</i>) (55)	62
Dodecanal	Pyridine	Room, then water bath	$n-C_{11}H_{23}CH=CHCO_2H$ (57)	308
Tridecanal	"	Steam bath	$n-C_{12}H_{25}CH=CHCO_2H$ (—)	327
11-Carbomethoxyundecanal	"	Room, then steam bath	$HO_2C(CH_2)_{10}CH=CHCO_2H^†$ (30–50)	325
	$C_6H_5N(CH_3)_2$	"	$HO_2C(CH_2)_9CH=CHCH_2CO_2H^†$ (—)	325
Pentadecanal	Pyridine	Room	$n-C_{14}H_{29}CH=CHCO_2H$ (50)	327
Tetracosanal	Piperidine + pyridine	60°, then boil	$n-C_{23}H_{47}CH=CHCO_2H$ (Poor)	322
B. Alicyclic Aldehydes or Ketones				
Cyclopropanecarboxaldehyde	Pyridine	B.p.	 $CH=CHCO_2H$ (56)	328
Cyclopentanecarboxaldehyde	Piperidine + pyridine	30–40°	$C_5H_9CH=CHCO_2H$ (33)	329
Cyclohexene-4-carboxaldehyde	Pyridine	Steam bath	 $CH=CHCO_2H$ (81)	330
Cyclohexanecarboxaldehyde	Piperidine + pyridine	Steam bath, then boil	$C_6H_{11}CH=CHCO_2H$ (80)	74
	$(C_2H_5)_2NH^†$	Room, then b.p.	$C_6H_{11}CH(CH_2CO_2H)_2$ (60)	74
	Pyridine	Room, then steam bath	$C_6H_{11}CH=CHO_2HC$ (80)	331
	$(HOCH_2CH_2)_2N$	"	 $CHCH_2CO_2H$ (35)	331
Cyclohexanonecarboxaldehyde imine	NH_3/C_2H_5OH	B.p.	$C_6H_{11}CH(NH_2)CH_2CO_2H$ (66) $C_6H_{11}CH=CHCO_2H$ (11)	332
Bicyclo[2,2,1]hept-2-ene-6-carboxaldehyde	Piperidine + pyridine	Steam bath, then boil	 $CH=CHCO_2H$ (87)	333
1-Methylcyclohexene-3-carboxaldehyde	Pyridine	110°	 $CH=CHCO_2H$ (18)	335
1-Methylcyclohexene-4-carboxaldehyde	Piperidine + pyridine	Steam bath, then boil	 $CH=CHCO_2H$ (76)	333
4-Methylcyclohexene-5-carboxaldehyde	"	—	 $CH=CHCO_2H$ (—)	334
1,2-Dimethylcyclohexene-4-carboxaldehyde	"	Steam bath, then b.p.	 $CH=CHCO_2H$ (95)	333
 $CH=CHCHO$	Pyridine	110°	 $CH=CHCH=CHCO_2H$ (63)	335
 $CH=CHCHO$	Piperidine + pyridine	40–50° then 100°	 $CH=CHCH=CHCO_2H$ (15)	336

Note: References 285 to 1153 are on pp. 582–599.

[†] The crude product was hydrolyzed.

[†] Diethylamine in alcohol gave a compound formulated as the lactone.

TABLE I—Continued
CONDENSATIONS WITH MALONIC ACID

B. Alicyclic Aldehydes or Ketones—Continued				
Aldehyde or Ketone	Catalyst	Temperature	Product(s) and Yield(s) (%)	Refs.
Hydroxymethylenecamphor	Pyridine	Water bath	 (—)	132
	"	110°	 (56)	335
	Piperidine	Room, then heat	 (70)	336
 <i>cis: syn: cis</i>	Piperidine + pyridine	0°, then steam bath	 <i>trans: syn: cis</i> and <i>cis: syn: cis</i>	78
	"	80–90°	 (—)	337
 <i>cis: syn: cis</i>	"	0°, then steam bath	 (36) (A) <i>trans: syn: cis</i> (+ <i>trans: syn: cis</i> form of starting material)	78
 <i>trans: syn: cis</i>	"	0°, then steam bath	(A) (p. 280) (32)	78
	"	Room, then heat	 (50)	336
	"	110°	 (70)	335
	"	80–90°	 (—)	337
 <i>(trans: syn: cis)</i>	"	0°, then steam bath	 (40) <i>(cis: syn: cis)</i>	78
	"	Room, then heat	 (64)	336

Note: References 285 to 1151 are on pp. 582–599.

* The double bond in the ring may be in either of the two positions indicated.

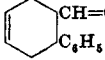
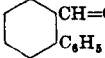
TABLE I—Continued
CONDENSATIONS WITH MALONIC ACID

282

ORGANIC REACTIONS

THE KNOEVENAGEL CONDENSATION

283

C. Aromatic Aldehydes or Ketones				
Aldehyde or Ketone	Catalyst	Temperature	Product(s) and Yield(s) (%)	Refs.
$C_6H_5COCF_3$	Piperidine + pyridine	B.p.	$C_6H_5C(CF_3)(OH)CH_2CO_2H$ (59)	35
2-Nitrophenylglyoxal	Pyridine	Room	$2-O_2NC_6H_4COCH=CHCO_2H$ (11)	86
3-Nitrophenylglyoxal	"	"	$3-O_2NC_6H_4COCH=CHCO_2H$ (23)	86
4-Nitrophenylglyoxal	"	"	$4-O_2NC_6H_4COCH=CHCO_2H$ (41)	86
$2-O_2NC_6H_4CH_2CHO$	Pyridine or none	Water bath, then 110°	$2-O_2NC_6H_4CH=CHCH_2CO_2H$ (—)	338
Phenylacetaldehyde	Pyridine	Water bath	$C_6H_5CH_2CH=CHCO_2H$ (50-55)	339
	$(C_2H_5)_2NH$	Boiling C_2H_5OH	$C_6H_5CH=CHCH_2CO_2H$ (60)	340
$2-O_2NC_6H_4CH=CHCHO$	Piperidine + pyridine	100°, then 130°	$2-O_2NC_6H_4(CH=CH)_2CO_2H$ (25)	87
			$2-O_2NC_6H_4CH=CHCH=C(CO_2H)_2$ (35)	
Cinnamaldehyde	Aniline	Water bath	$C_6H_5(CH=CH)_2CO_2H$ (70)	7
	NH_3/C_2H_5OH	B.p.	$C_6H_5CH=CHCH=C(CO_2H)_2$ (60)	7
	Pyridine	Room	$C_6H_5CH=CHCH=C(CO_2H)_2$ (—)	13
	"	Water bath	$C_6H_5(CH=CH)_2CO_2H$ (40)	13
	"	" "	$C_6H_5CH=CHCH=C(CO_2H)_2$ (96)	291, 341
			or $C_6H_5(CH=CH)_2CO_2H^1$ (55)	
	$(C_2H_5)_2NH$	" "	$C_6H_5CH=CHCH=C(CO_2H)_2$ (—)	121
	Piperidine + pyridine	B.p.	$C_6H_5(CH=CH)_2CO_2H$ (60)	285
	"	Steam bath	$C_6H_5CH=CHCH=C(CO_2H)_2$ (66)	342
	Quinoline	85°	$C_6H_5CH=CHCH=C(CO_2H)_2$ (76)	259
	$(HOCH_2CH_2)_3N$	Water bath	$C_6H_5CH=CHCH=C(CO_2H)_2$ (Poor)	58
$C_6H_5CH=CHCH(OC_2H_5)_2$	Piperidine + pyridine	100°, then 140°	$C_6H_5(CH=CH)_2CO_2H$ (17)	87
			$C_6H_5CH=CHCH=C(CO_2H)_2$ (27)	
2-Phenylpropionaldehyde (hydratropaldehyde)	$(C_2H_5)_2NH$	Boiling C_2H_5OH	$C_6H_5CH(CH_3)CH=CHCO_2H$ (—)	344
3-Phenylpropionaldehyde	Pyridine	Water bath	$C_6H_5CH_2CH_2CH=CHCO_2H$ (29)	291
	"	180°	$C_6H_5CH_2CH_2CH=CHCO_2H$ (55)	343
2-Methoxycinnamaldehyde	Piperidine + pyridine	Steam bath	$2-CH_3OC_6H_4CH=CHCH=C(CO_2H)_2$ (100)	342
4-Methoxycinnamaldehyde	$NH_3/C_2H_5OH/H_2O$	B.p.	$4-CH_3OC_6H_4CH=CHCH=C(CO_2H)_2$ (—)	345
	Piperidine + pyridine	Steam bath, then boil	$4-CH_3OC_6H_4(CH=CH)_2CO_2H$ (40)	345
	"	Steam bath	$4-CH_3OC_6H_4CH=CHCH=C(CO_2H)_2$ (76)	342
5-Phenyl-2,4-pentadienal	$NH_3/C_2H_5OH/H_2O$	B.p.	$C_6H_5(CH=CH)_2CH=C(CO_2H)_2$ (60)	346
$C_6H_5COCOCOC_2H_5$	Piperidine + pyridine	Water bath	$C_6H_5COC(OH)CH_2CO_2H$ $CO_2C_2H_5$ (40)	347
$C_6H_5CH(CO_2C_2H_5)CHO$	Pyridine	Water bath	$C_6H_5C(CO_2C_2H_5)=CHCH_2CO_2H$ (60)	132
3,4-Dimethoxycinnamaldehyde	Piperidine + pyridine	Steam bath	$3,4-(CH_3O)_2C_6H_3CH=CHCH=C(CO_2H)_2$ (57)	342
1-Naphthylglyoxal	Pyridine	Room	$1-C_{10}H_7COCH=CHCO_2H$ (53)	86
2-Naphthylglyoxal	"	Room	$2-C_{10}H_7COCH=CHCO_2H$ (45)	86, 348
4-Phenylcyclohexene-5-carboxaldehyde	Piperidine + pyridine	100°, then 150°	 C_6H_5 (53)	349
2-Phenylcyclohexane-1-carboxaldehyde	"	100°, then 150°	 C_6H_5 (72)	349
4-Biphenylacetaldehyde	Pyridine	Boiling C_2H_5OH	$4-C_6H_5C_6H_4CH_2CH=CHCO_2H$ (21)	350, 351
1,3-Diphenylpropanetrione	Piperidine + pyridine	5°, then room	$(C_6H_5CO)_2C(OH)CH(CO_2H)_2$ (44)	352
3-Cyano-3,3-diphenylpropionaldehyde	"	B.p.	$(C_6H_5)_3C(CN)CH_2CH=CHCO_2H$ (80)	353
11-Phenylundecapentaenal	"	Water bath	$C_6H_5(CH=CH)_4CO_2H$ (—)	1133
3-Cyano-3-cyclohexyl-3-phenylpropionaldehyde	"	B.p.	$C_6H_5(C_6H_{11})C(CN)CH_2CH=CHCO_2H$ (65-70)	353
4-Cyano-4,4-diphenylbutyraldehyde	"	B.p.	$(C_6H_5)_2C(CN)CH_2CH_2CH=CHCO_2H$ (65)	353
D. Aromatic Aldehydes or Ketones				
Pentafluorobenzaldehyde	Pyridine	100°	$C_6F_5CH=CHCO_2H$ (45)	354
2,4,6-Tribromo-3-hydroxybenzaldehyde	"	Water bath	$2,4,6-Br_3-3-HOC_6H_2CH=C(CO_2H)_2$ (93)	355
2,4,6-Trichloro-3-hydroxybenzaldehyde	"	105-110°	$2,4,6-Cl_3-3-HOC_6H_2CH=C(CO_2H)_2$ (100)	355
2,4,6-Triiodo-3-hydroxybenzaldehyde	"	Boiling C_2H_5OH	$2,4,6-I_3-3-HOC_6H_2CH=C(CO_2H)_2$ (70)	355
2-Chloro-3,5-dinitrobenzaldehyde	Pyridine or piperidine	Water bath	$2-Cl-3,5-(O_2N)_2C_6H_2CH=CHCO_2H$ (90)	1134
4-Chloro-3,5-dinitrobenzaldehyde	Piperidine, pyridine, or quinoline	Heat	$4-Cl-3,5-(O_2N)_2C_6H_2CH=CHCO_2H$ (89-92)	356

Note: References 285 to 1153 are on pp. 582-599.

¹ The length of heating determines the product.

TABLE I—Continued
CONDENSATIONS WITH MALONIC ACID

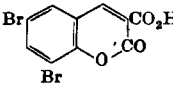
284

ORGANIC REACTIONS

THE KNOEVENAGEL CONDENSATION

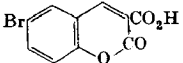
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D. Aromatic Aldehydes or Ketones—Continued

Aldehyde or Ketone	Catalyst	Temperature	Product(s) and Yield(s) (%)	Refs.
3,5-Dibromo-2-hydroxybenzaldehyde	Pyridine	110°	3,5-Br ₂ -2-HOC ₆ H ₃ CH=CHCO ₂ H (31) 3,5-Br ₂ -2-HOC ₆ H ₃ CH=C(CO ₂ H) ₂ (22)	357
	None	Water bath, then 130°	 (76)	357
3,5-Dibromo-4-hydroxybenzaldehyde	Pyridine	Boiling C ₂ H ₅ OH	3,5-Br ₂ -4-HOC ₆ H ₃ CH=C(CO ₂ H) ₂ (87)	358
2,4-Cl ₂ C ₆ H ₃ CHO	"	Boiling C ₂ H ₅ OH	2,4-Cl ₂ C ₆ H ₃ CH=CHCO ₂ H (70)	360
2,4-Cl ₂ C ₆ H ₃ CH(OC ₂ H ₅) ₂	Piperidine + pyridine	100°, then 130°	2,4-Cl ₂ C ₆ H ₃ CH=CHCO ₂ H (15)	87
2,6-Cl ₂ C ₆ H ₃ CHO	"	Water bath	2,6-Cl ₂ C ₆ H ₃ CH=CHCO ₂ H (34)	359
3,4-Cl ₂ C ₆ H ₃ CHO	"	90°	3,4-Cl ₂ C ₆ H ₃ CH=CHCO ₂ H (—)	361
	Pyridine	Boiling C ₂ H ₅ OH	3,4-Cl ₂ C ₆ H ₃ CH=CHCO ₂ H (81)	360
3,4-Cl ₂ C ₆ H ₃ CH(OC ₂ H ₅) ₂	Piperidine + pyridine	100°, then 130°	3,4-Cl ₂ C ₆ H ₃ CH=CHCO ₂ H (71)	87
3,5-Cl ₂ C ₆ H ₃ CHO	"	Water bath, then 160°	3,5-Cl ₂ C ₆ H ₃ CH=CHCO ₂ H (<i>trans</i>) (95) ^f	362
2,6-Dichloro-3-hydroxybenzaldehyde	Pyridine	Boiling C ₂ H ₅ OH	2,6-Cl ₂ -3-HOC ₆ H ₃ CH=CHCO ₂ H (91)	355
3,5-Dichloro-4-hydroxybenzaldehyde	Pyridine	" "	3,5-Cl ₂ -4-HOC ₆ H ₃ CH=C(CO ₂ H) ₂ (75)	358
3,5-Diiodo-4-hydroxybenzaldehyde	"	" "	3,5-I ₂ -4-HOC ₆ H ₃ CH=C(CO ₂ H) ₂ (81)	358
2,4-(O ₂ N) ₂ C ₆ H ₃ CHO	"	Water bath, then 110°	2,4-(O ₂ N) ₂ C ₆ H ₃ CH=CHCO ₂ H (50)	363
3-Br-6-O ₂ NC ₆ H ₃ CHO	Piperidine + pyridine	95°, then boil	3-Br-6-O ₂ NC ₆ H ₃ CH=CHCO ₂ H (84)	364
3-Cl-6-O ₂ NC ₆ H ₃ CHO	"	" "	3-Cl-6-O ₂ NC ₆ H ₃ CH=CHCO ₂ H (70)	364
3-BrC ₆ H ₄ CHO	"	B.p.	3-BrC ₆ H ₄ CH=CHCO ₂ H (83)	285
	Pyridine	Water bath or boiling C ₂ H ₅ OH	3-BrC ₆ H ₄ CH=CHCO ₂ H (97;31)	365, 360
	None	Water bath	3-BrC ₆ H ₄ CH=C(CO ₂ H) ₂ (99)	365
4-BrC ₆ H ₄ CHO	Pyridine	Boiling C ₂ H ₅ OH	4-BrC ₆ H ₄ CH=CHCO ₂ H (60)	366
	Piperidine + pyridine	Steam bath	4-BrC ₆ H ₄ CH=CHCO ₂ H (94)	367
3-Br-4-HOC ₆ H ₃ CHO	Pyridine	Boiling C ₂ H ₅ OH	3-Br-4-HOC ₆ H ₃ CH=C(CO ₂ H) ₂ (75)	358
3-Br-6-HOC ₆ H ₃ CHO	"	Steam bath	3-Br-6-HOC ₆ H ₃ CH=CHCO ₂ H (50) ^m	357
	"	" "	3-Br-6-HOC ₆ H ₃ CH=C(CO ₂ H) ₂ (20-25)	
4-Br-3-HOC ₆ H ₃ CHO	"	Water bath	4-Br-3-HOC ₆ H ₃ CH=CHCO ₂ H (92)	355
2-ClC ₆ H ₄ CHO	Quinoline	85°	2-ClC ₆ H ₄ CH=CHCO ₂ H (71)	259
	Piperidine + pyridine	Steam bath, then 130°	2-ClC ₆ H ₄ CH=CHCO ₂ H (71)	368
	Pyridine	Water bath or boiling C ₂ H ₅ OH	2-ClC ₆ H ₄ CH=CHCO ₂ H (82)	360, 365, 366
	None	" "	2-ClC ₆ H ₄ CH=C(CO ₂ H) ₂ (93)	365
3-ClC ₆ H ₄ CHO	Piperidine + pyridine	Water bath	3-ClC ₆ H ₄ CH=CHCO ₂ H (<i>trans</i>) (91)	362
	Pyridine	Water bath or boiling C ₂ H ₅ OH	3-ClC ₆ H ₄ CH=CHCO ₂ H (53-100)	360, 365
	None	Water bath	3-ClC ₆ H ₄ CH=C(CO ₂ H) ₂ (Quant.)	365
4-ClC ₆ H ₄ CHO	None	Water bath	4-ClC ₆ H ₄ CH=C(CO ₂ H) ₂ (Quant.)	365
	Pyridine	Water bath or boiling C ₂ H ₅ OH	4-ClC ₆ H ₄ CH=CHCO ₂ H (73)	360, 365, 366
	Piperidine + pyridine	Steam bath, then boil	4-ClC ₆ H ₄ CH=CHCO ₂ H (97)	298
2-Cl-3-HOC ₆ H ₃ CHO	Pyridine	Boiling C ₂ H ₅ OH	2-Cl-3-HOC ₆ H ₃ CH=CHCO ₂ H (96)	84
3-Cl-4-HOC ₆ H ₃ CHO	"	" "	3-Cl-4-HOC ₆ H ₃ CH=C(CO ₂ H) ₂ (57)	358
2-FC ₆ H ₄ CHO	"	" "	2-FC ₆ H ₄ CH=CHCO ₂ H (78)	366, 369
3-FC ₆ H ₄ CHO	NH ₃ /C ₂ H ₅ OH	Cold, then warm	3-FC ₆ H ₄ CH=CHCO ₂ H (49)	370
4-FC ₆ H ₄ CHO	CH ₃ CO ₂ NH ₄	Boiling ethanol	4-FC ₆ H ₄ CH(NH ₂)CH ₂ CO ₂ H (67) 4-FC ₆ H ₄ CH=CHCO ₂ H (15)	371
4-I-3-HOC ₆ H ₃ CHO	Pyridine	Water bath	4-I-3-HOC ₆ H ₃ CH=CHCO ₂ H (93)	355
2-O ₂ NC ₆ H ₄ CHO	Aniline ⁿ	" "	2-O ₂ NC ₆ H ₄ CH=CHCO ₂ H (50)	7, 18
	C ₆ H ₅ NH ₂ /C ₂ H ₅ OH	Room	2-O ₂ NC ₆ H ₄ CH=C(CO ₂ H) ₂ (80)	18
	Piperidine + pyridine	Boiling point	2-O ₂ NC ₆ H ₄ CH=CHCO ₂ H (73)	285, 372
	Quinoline	85°	2-O ₂ NC ₆ H ₄ CH=CHCO ₂ H (44)	259
	Pyridine	Water bath	2-O ₂ NC ₆ H ₄ CH=CHCO ₂ H (91-96)	291, 373

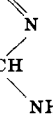

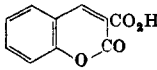
Note: References 285 to 1153 are on pp. 582-599.

^f The yield given is of crude product.

^m With no catalyst 92% of  was obtained.

ⁿ A number of other organic bases were used but gave lower yields.

TABLE I—Continued
CONDENSATIONS WITH MALONIC ACID

D. Aromatic Aldehydes or Ketones—Continued				
Aldehyde or Ketone	Catalyst	Temperature	Product(s) and Yield(s)	Refs.
3-O ₂ NC ₆ H ₄ CHO	Alcoholic NH ₃	60–70°	3-O ₂ NC ₆ H ₄ CH=C(CO ₂ H) ₂ (59)	7
	NH ₃ /C ₂ H ₅ OH	Water bath	3-O ₂ NC ₆ H ₄ CH(NH ₂)CH ₂ CO ₂ H (61)	20
			3-O ₂ NC ₆ H ₄ CH=CHCO ₂ H ^a (34)	
	Piperidine + pyridine	Boiling point or water bath	3-O ₂ NC ₆ H ₄ CH=CHCO ₂ H (90)	273, 285, 372, 374–376
	Aniline	Room	3-O ₂ NC ₆ H ₄ CH=C(CO ₂ H) ₂ (—)	18
	"	Water bath	3-O ₂ NC ₆ H ₄ CH=CHCO ₂ H (—)	18
	Quinoline	85°	3-O ₂ NC ₆ H ₄ CH=CHCO ₂ H (82)	259
4-O ₂ NC ₆ H ₄ CHO	Pyridine	Water bath or boiling C ₂ H ₅ OH	3-O ₂ NC ₆ H ₄ CH=CHCO ₂ H (90)	291, 360, 373, 377
	CH ₂ (CO ₂ NH ₄) ₂	60–70°	4-O ₂ NC ₆ H ₄ CH=C(CO ₂ H) ₂ (54)	7
	Alcoholic NH ₃	Water bath	4-O ₂ NC ₆ H ₄ CH=CHCO ₂ H (92)	7
	Aniline	Room	4-O ₂ NC ₆ H ₄ CH=C(CO ₂ H) ₂ (80)	18
	"	Water bath	4-O ₂ NC ₆ H ₄ CH=CHCO ₂ H (50)	18
	Piperidine + pyridine	Boiling point	4-O ₂ NC ₆ H ₄ CH=CHCO ₂ H (82)	285
	Pyridine	Water bath	4-O ₂ NC ₆ H ₄ CH=CHCO ₂ H (87–90)	291, 373
2-Nitro-5-hydroxybenzaldehyde	Quinoline	85°	4-O ₂ NC ₆ H ₄ CH=CHCO ₂ H (75)	259
	Piperidine + pyridine	Steam bath, then boil	2-O ₂ N-5-HOC ₆ H ₃ CH=CHCO ₂ H (—)	378
3-Nitro-2-hydroxybenzaldehyde	"	Water bath	3-O ₂ N-2-HOC ₆ H ₃ CH=C(CO ₂ H) ₂ (53)	379
5-Nitro-2-hydroxybenzaldehyde	Pyridine	80°	5-O ₂ N-2-HOC ₆ H ₃ CH=CHCO ₂ H (69)	380
4-Nitro-3-hydroxybenzaldehyde	Piperidine + pyridine	Steam bath, then boil	4-O ₂ N-3-HOC ₆ H ₃ CH=CHCO ₂ H (—)	378
Benzaldehyde	Alcoholic NH ₃ , piperidine, or tri-ethanolamine	60–70°, or room	C ₆ H ₅ CH=C(CO ₂ H) ₂ (59)	7, 18, 58, 121, 381–383
	Aniline, piperidine, or alcoholic NH ₃ ^p	Water bath	C ₆ H ₅ CH=CHCO ₂ H (80–90)	7
	Piperidine + pyridine	B.p.	C ₆ H ₅ CH=CHCO ₂ H (95)	285, 359
	Quinoline	85°	C ₆ H ₅ CH=CHCO ₂ H (80)	259
	Pyridine	Steam bath	C ₆ H ₅ CH=CHCO ₂ H (83–95)	291, 365
	None	" "	C ₆ H ₅ CH=C(CO ₂ H) ₂ (78)	365
			C ₆ H ₅ CH	
				
	Hydrobenzamide	Room (in ether)	C ₆ H ₅ CH (65)	19
				
Benzaldehyde diethyl acetal	Alcoholic NH ₃	B.p.	C ₆ H ₅ CHCH(CO ₂ H) ₂	
	Ethanolamine	B.p.	C ₆ H ₅ CH(NH ₂)CH ₂ CO ₂ H (50)	20
	Piperidine + pyridine	100°, then 130°	C ₆ H ₅ CH=CHCO ₂ H (30)	382
			C ₆ H ₅ CH=CHCO ₂ H (61)	87
Salicylaldehyde			C ₆ H ₅ CH=CHCO ₂ H (89)	
	C ₆ H ₅ NH ₂ or C ₆ H ₅ NH ₃ Cl	Water bath or room	 (83)	7, 18, 80, 305
	Pyridine, or pyridine + piperidine	60°, or b.p.	(Coumarin-3-carboxylic acid)	
	Methylacridine (and other bases)	80°	Coumarin-3-carboxylic acid ^q (20)	84, 285, 291
			Coumarin-3-carboxylic acid (77)	384
	HOCH ₂ CH ₂ NH ₂ /C ₂ H ₅ OH	Room	Coumarin-3-carboxylic acid (76)	382
	CH ₃ CO ₂ NH ₄	Boiling C ₂ H ₅ OH	Coumarin-3-carboxylic acid (—)	385
3-HOC ₆ H ₄ CHO	Quinoline	85°	3-HOC ₆ H ₄ CH=CHCO ₂ H (70)	259
	Pyridine, or piperidine + pyridine	110–115°	3-HOC ₆ H ₄ CH=CHCO ₂ H (89)	376, 386

Note: References 285 to 1153 are on pp. 582–599.

^a Knoevenagel reported that the cinnamic acid was obtained in 72% yield.⁷

^p Six other organic catalysts gave inferior yields.

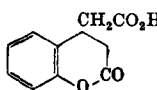
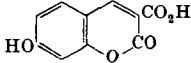
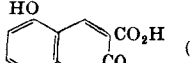
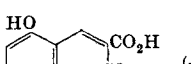
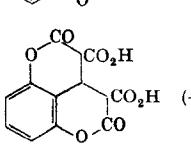
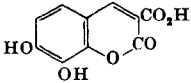
^q Two other products, *o*-HOC₆H₄CH(CH₂CO₂H)₂ and  were also isolated.⁸⁴

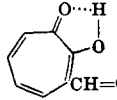
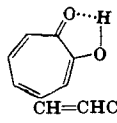
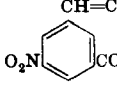
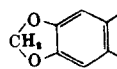
TABLE I—Continued
CONDENSATIONS WITH MALONIC ACID

D. Aromatic Aldehydes or Ketones—Continued				
Aldehyde or Ketone	Catalyst	Temperature	Product(s) and Yield(s) (%)	Refs.
3-HOC ₆ H ₄ CHO (<i>contd.</i>)	Aniline + pyridine	55°	3-HOC ₆ H ₄ CH=CHCO ₂ H (90)	80
	Pyridinium acetate	Water bath	3-HOC ₆ H ₄ CH=CHCO ₂ H (99)	355
	CH ₃ CO ₂ NH ₄	Boiling n-C ₄ H ₉ OH	3-HOC ₆ H ₄ CH(NH ₂)CH ₂ CO ₂ H (52)	385
4-HOC ₆ H ₄ CHO	Pyridine	Water bath or boiling C ₆ H ₆	4-HOC ₆ H ₄ CH=CHCO ₂ H (64–73)	291, 387, 388
	Quinoline	85°	4-HOC ₆ H ₄ CH=CHCO ₂ H (10)	259
	Aniline + pyridine	65°, room	4-HOC ₆ H ₄ CH=CHCO ₂ H (84)	80, 389–391
	Piperidine + pyridine	37°	4-HOC ₆ H ₄ CH=CHCO ₂ H (78)	392
	CH ₃ CO ₂ NH ₄	Boiling n-C ₄ H ₉ OH	4-HOC ₆ H ₄ CH(NH ₂)CH ₂ CO ₂ H (21)	385
2,4-(HO) ₂ C ₆ H ₃ CHO	Pyridine	Water bath	4-HOC ₆ H ₄ CH=CHCO ₂ H (—)	
			2,4-(HO) ₂ C ₆ H ₃ CH=CHCO ₂ H (43)	393
	Aniline + pyridine	55°	 (71)	80
2,6-(HO) ₂ C ₆ H ₃ CHO	" "	25°	 (83)	80
	Pyridine or morpholine	Mild	 (—)	394
	" "	Vigorous	 (—)	394
3,4-Dihydroxybenzaldehyde (protocatechuic aldehyde)	Piperidine + pyridine	B.p.	3,4-(HO) ₂ C ₆ H ₃ CH=CHCO ₂ H (7)	285
	" "	10–25°	3,4-(HO) ₂ C ₆ H ₃ CH=CHCO ₂ H (83)	373
	Aniline + pyridine	Room, then 55°	3,4-(HO) ₂ C ₆ H ₃ CH=CHCO ₂ H (87)	80, 270
	CH ₃ CO ₂ NH ₄	Boiling C ₂ H ₅ OH	3,4-(HO) ₂ C ₆ H ₃ CH=CHCO ₂ H (—)	385
3,5-Dihydroxybenzaldehyde	Piperidine/C ₂ H ₅ OH	100°	3,5-(HO) ₂ C ₆ H ₃ CH=CHCO ₂ H (—)	395
2,3,4-Trihydroxybenzaldehyde	Aniline + pyridine	37°	 (83)	270
3,4,5-Trihydroxybenzaldehyde	Piperidine	Boiling C ₂ H ₅ OH	3,4,5-(HO) ₃ C ₆ H ₂ CH=CHCO ₂ H (50)	16
2-Nitro-4-aminobenzaldehyde	Pyridine	Boiling C ₂ H ₅ OH	2-O ₂ N-4-H ₂ NC ₆ H ₃ CH=CHCO ₂ H (—)	396
4-Sulfonamidobenzaldehyde	Piperidine + pyridine	100°	4-H ₂ NO ₂ SC ₆ H ₄ CH=CHCO ₂ H (67–87)	397
3,4-Difluoromethylene-dioxybenzaldehyde	" "	B.p.	3,4-CF ₂ O ₂ C ₆ H ₃ CH=CHCO ₂ H (70)	398
2-Bromo-4,5-methylene-dioxybenzaldehyde	" "	Water bath	2-Br-4,5-CH ₂ O ₂ C ₆ H ₃ CH=CHCO ₂ H (Quant.)	399
4-CF ₃ C ₆ H ₄ CHO	" "	Heat	4-CF ₃ C ₆ H ₄ CH=CHCO ₂ H (92)	398
2-Cyanobenzaldehyde	Pyridine	Boiling C ₂ H ₅ OH	2-NCC ₆ H ₄ CH=CHCO ₂ H (61)	369
	Piperidine + pyridine	80°, then 100°, then boil	2-NCC ₆ H ₄ CH=CHCO ₂ H (60–70)	400
3-Cyanobenzaldehyde	Pyridine	"	3-NCC ₆ H ₄ CH=CHCO ₂ H (71)	401
4-Cyanobenzaldehyde	Piperidine + pyridine	"	4-NCC ₆ H ₄ CH=CHCO ₂ H (83)	402
2-Nitroterephthalaldehyde	Pyridine	40–50°, then 90°	2-O ₂ NC ₆ H ₃ (CH=CHCO ₂ H) ₂ -1,4 (72)	403
2-Nitro-4,5-methylene-dioxybenzaldehyde	Piperidine + pyridine	100°, then boil	2-O ₂ N-4,5-CH ₂ O ₂ C ₆ H ₃ CH=CHCO ₂ H (96)	404
Phthalaldehyde	Pyridine	55–60°	2-OHCC ₆ H ₄ CH=CHCO ₂ H (67) ^r	405
Isophthalaldehyde	Piperidine	45–50°, then water bath	C ₆ H ₄ (CH=CHCO ₂ H) ₂ -1,3 (98)	406
	Pyridine	Water bath, then boil	C ₆ H ₄ (CH=CHCO ₂ H) ₂ -1,3 (84)	407
Terephthalaldehyde	Piperidine + pyridine	45–50°, then water bath	C ₆ H ₄ (CH=CHCO ₂ H) ₂ -1,4 (82)	408

Note: References 285 to 1153 are on pp. 582–599.

^r Equivalent amounts of aldehyde and malonic acid were used.

TABLE I—Continued
CONDENSATIONS WITH MALONIC ACID

D. Aromatic Aldehydes or Ketones—Continued				
Aldehyde or Ketone	Catalyst	Temperature	Product(s) and Yield(s) (%)	Refs.
Terephthalaldehyde (<i>contd.</i>)	Piperidine	Boiling C ₂ H ₅ OH	4-OHCC ₆ H ₄ CH=CHCO ₂ H (61) ^r C ₆ H ₄ (CH=CHCO ₂ H)-1,4 (—)	405
3,4-Methylenedioxybenzaldehyde (piperonal)	"	" "	C ₆ H ₄ (CH=CHCO ₂ H)-1,4 (70-80) ^a	405
	Alcoholic NH ₃	Water bath	3,4-CH ₂ O ₂ C ₆ H ₃ CH=CHCO ₂ H (85)	7, 409
	CH ₂ (CO ₂ NH ₄) ₂	60-70°	3,4-CH ₂ O ₂ C ₆ H ₃ CH=C(CO ₂ H) ₂ (60)	7
	Piperidine + pyridine	Boiling point or steam bath	3,4-CH ₂ O ₂ C ₆ H ₃ CH=CHCO ₂ H (100)	285, 410, 411-413
	" "	Room or 30-40°	3,4-CH ₂ O ₂ C ₆ H ₃ CH=CHCO ₂ H (97)	270, 414
	Aniline or piperidine in ethanol	Room	3,4-CH ₂ O ₂ C ₆ H ₃ CH=C(CO ₂ H) ₂ (40)	18
	Ethanol amines or ammonia	Steam bath	3,4-CH ₂ O ₂ C ₆ H ₃ CH(NRR')CH ₂ CO ₂ H + 3,4-CH ₂ O ₂ C ₆ H ₃ CH=CHCO ₂ H (—)	17, 20
	Quinoline	85°	3,4-CH ₂ O ₂ C ₆ H ₃ CH=CHCO ₂ H (89)	259, 415
	Pyridine	Water bath	3,4-CH ₂ O ₂ C ₆ H ₃ CH=CHCO ₂ H (100)	291, 415
	HOCH ₂ CH ₂ NH ₂	Room	3,4-CH ₂ O ₂ C ₆ H ₃ CH=C(CO ₂ H) ₂ (84)	382
Tropolone-3-carboxaldehyde	Pyridine	Water bath	 (—)	416
Tropolone-4-carboxaldehyde	Piperidine + pyridine	Steam bath	 (—)	417
3-Nitro-5-carboxybenzaldehyde	" "	70-80°, then 140°	 (84)	418
2-Hydroxy-4,5-methylene-dioxybenzaldehyde	Aniline + pyridine	55°	 (71)	419
2-Br-5-CH ₃ C ₆ H ₃ CHO	Piperidine + pyridine	(—)	2-Br-5-CH ₃ C ₆ H ₃ CH=CHCO ₂ H (—)	420
2-Br-4-CH ₃ OC ₆ H ₃ CHO	Pyridine	Boiling C ₂ H ₅ OH	2-Br-4-CH ₃ OC ₆ H ₃ CH=CHCO ₂ H (70)	421
3-Br-4-CH ₃ OC ₆ H ₃ CHO	Piperidine + pyridine	100°	3-Br-4-CH ₃ OC ₆ H ₃ CH=CHCO ₂ H (—)	423
2-Cl-4-CH ₃ C ₆ H ₃ CHO	Pyridine	Steam bath	2-Cl-4-CH ₃ C ₆ H ₃ CH=CHCO ₂ H (21)	422
3-Cl-6-CH ₃ C ₆ H ₃ CHO	Piperidine + pyridine	(—)	3-Cl-6-CH ₃ C ₆ H ₃ CH=CHCO ₂ H (—)	420
3-Cl-4-CH ₃ OC ₆ H ₃ CHO	" "	100°	3-Cl-4-CH ₃ OC ₆ H ₃ CH=CHCO ₂ H (—)	423
3-Chloro-4-hydroxy-5-methoxybenzaldehyde	" "	Room	3-Cl-4-HO-5-CH ₃ OC ₆ H ₃ CH=CHCO ₂ H (98)	414
3-F-4-CH ₃ OC ₆ H ₃ CHO	CH ₃ CO ₂ NH ₄	Boiling C ₂ H ₅ OH	3-F-4-CH ₃ OC ₆ H ₃ CH(NH ₂)CH ₂ CO ₂ H (58)	371
3-I-4-CH ₃ OC ₆ H ₃ CHO	Piperidine + pyridine	100°	3-F-4-CH ₃ OC ₆ H ₃ CH=CHCO ₂ H (23)	423
2-O ₂ N-5-CH ₃ C ₆ H ₃ CHO	" "	Heat	3-I-4-CH ₃ OC ₆ H ₃ CH=CHCO ₂ H (—)	424 (see 425)
2-O ₂ N-3-CH ₃ OC ₆ H ₃ CHO	" "	Steam bath, then boil	2-O ₂ N-5-CH ₃ C ₆ H ₃ CH=CHCO ₂ H (—)	378
2-O ₂ N-5-CH ₃ OC ₆ H ₃ CHO	" "	Steam bath, then boil	2-O ₂ N-3-CH ₃ OC ₆ H ₃ CH=CHCO ₂ H (Almost quant.)	378
3-O ₂ N-4-CH ₃ OC ₆ H ₃ CHO	" "	Water bath	2-O ₂ N-5-CH ₃ OC ₆ H ₃ CH=CHCO ₂ H (Almost quant.)	378
4-O ₂ N-3-CH ₃ OC ₆ H ₃ CHO	" "	Steam bath, then boil	3-O ₂ N-4-CH ₃ OC ₆ H ₃ CH=CHCO ₂ H (82)	372
3-Nitro-4-hydroxy-5-methoxybenzaldehyde	" "	Room or steam bath	4-O ₂ N-3-CH ₃ OC ₆ H ₃ CH=CHCO ₂ H (Almost quant.)	378
2-CH ₃ C ₆ H ₄ CHO	" "	Steam bath	3-O ₂ N-4-HO-5-CH ₃ OC ₆ H ₃ CH=CHCO ₂ H (90)	414, 426
			2-CH ₃ C ₆ H ₄ CH=CHCO ₂ H (75)	427

Note: References 285 to 1153 are on pp. 582-599.

^r Equivalent amounts of aldehyde and malonic acid were used.

^a A 2:1 ratio of acid to aldehyde was used.

TABLE I—Continued
CONDENSATIONS WITH MALONIC ACID

292

ORGANIC REACTIONS

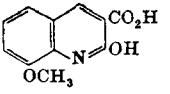
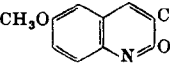
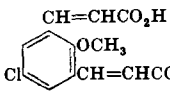
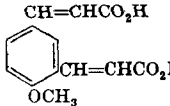
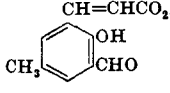
THE KNOEVENAGEL CONDENSATION

293

D. Aromatic Aldehydes or Ketones—Continued				
Aldehyde or Ketone	Catalyst	Temperature	Product(s) and Yield(s) (%)	Refs.
3-CH ₃ C ₆ H ₄ CHO	None	Water bath	3-CH ₃ C ₆ H ₄ CH=C(CO ₂ H) ₂ (20–32)	428
	Piperidine + pyridine	Room	3-CH ₃ C ₆ H ₄ CH=CHCO ₂ H (Quant.)	428
	" "	60°, then 105°	3-CH ₃ C ₆ H ₄ CH=CHCO ₂ H (78)	429
4-CH ₃ C ₆ H ₄ CHO	" "	B.p.	4-CH ₃ C ₆ H ₄ CH=CHCO ₂ H (87)	285, 430
	Pyridine	Water bath	4-CH ₃ C ₆ H ₄ CH=CHCO ₂ H (99)	291, 373, 428
	Quinoline	85°	4-CH ₃ C ₆ H ₄ CH=CHCO ₂ H (69)	259
4-CH ₃ C ₆ H ₄ CH			4-CH ₃ C ₆ H ₄ CH	
4-CH ₃ C ₆ H ₄ CH			4-CH ₃ C ₆ H ₄ CH	
4-CH ₃ C ₆ H ₄ CH			4-CH ₃ C ₆ H ₄ CH	
4-CH ₃ C ₆ H ₄ CH(OC ₂ H ₅) ₂	Piperidine + pyridine	100°, then 130°	4-CH ₃ C ₆ H ₄ CH=CHCO ₂ H (Quant.)	87
2-CH ₃ OC ₆ H ₄ CHO	" "	Water bath	2-CH ₃ OC ₆ H ₄ CH=CHCO ₂ H (80)	412, 431
	Pyridine	B.p. or boiling	2-CH ₃ OC ₆ H ₄ CH=CHCO ₂ H (100)	360, 432, 433
	CH ₃ CO ₂ NH ₄	Boiling C ₂ H ₅ OH	2-CH ₃ OC ₆ H ₄ CH=CHCO ₂ H (—)	385
	NH ₃ /C ₂ H ₅ OH	—	2-CH ₃ OC ₆ H ₄ CH=CHCO ₂ H (43)	434
2-CH ₃ OC ₆ H ₄ CH(OC ₂ H ₅) ₂	Piperidine + pyridine	100°, then 140°	2-CH ₃ OC ₆ H ₄ CH=CHCO ₂ H (Quant.)	87
3-CH ₃ OC ₆ H ₄ CHO	" "	Water bath (and reflux)	3-CH ₃ OC ₆ H ₄ CH=CHCO ₂ H (Almost quant.)	412, 435, 436, 437, 439
	Pyridine	Boiling C ₂ H ₅ OH or pyridine	3-CH ₃ OC ₆ H ₄ CH=CHCO ₂ H (84)	377, 433
4-CH ₃ OC ₆ H ₄ CHO	CH ₃ CO ₂ NH ₄	Boiling C ₂ H ₅ OH	3-CH ₃ OC ₆ H ₄ CH(NH ₂)CH ₂ CO ₂ H (62)	385
	NH ₃ /C ₂ H ₅ OH	Water bath	4-CH ₃ OC ₆ H ₄ CH=CHCO ₂ H (91)	7
	CH ₂ (CO ₂ NH ₄) ₂	60–70°	4-CH ₃ OC ₆ H ₄ CH=C(CO ₂ H) ₂ (66)	7
	C ₅ H ₁₁ NH ₂	Water bath	4-CH ₃ OC ₆ H ₄ CH=C(CO ₂ H) ₂ (Quant.)	121
	Piperidine + pyridine	Water bath or b.p.	4-CH ₃ OC ₆ H ₄ CH=CHCO ₂ H (Quant.)	285, 361, 412, 434, 438, 439–441
	C ₆ H ₅ NH ₂ /C ₂ H ₅ OH	Room	4-CH ₃ OC ₆ H ₄ CH=C(CO ₂ H) ₂ (—)	18
	Quinoline	85°	4-CH ₃ OC ₆ H ₄ CH=CHCO ₂ H (72)	259, 442
	Pyridine	Boiling C ₂ H ₅ OH or water bath	4-CH ₃ OC ₆ H ₄ CH=CHCO ₂ H (60)	291, 360, 442–445
	CH ₃ CO ₂ NH ₄	Boiling C ₂ H ₅ OH or n-C ₄ H ₉ OH	4-CH ₃ OC ₆ H ₄ CH(NH ₂)CH ₂ CO ₂ H (54)	385, 446
4-CH ₃ OC ₆ H ₄ CH(OC ₂ H ₅) ₂	Piperidine + pyridine	100°, then 140°	4-CH ₃ OC ₆ H ₄ CH=CHCO ₂ H (Quant.)	87
3-HO-4-CH ₃ C ₆ H ₃ CHO	Aniline + pyridine	20°, then 80°	3-HO-4-CH ₃ C ₆ H ₃ CH=CHCO ₂ H (92)	447
4-HO-2-CH ₃ C ₆ H ₃ CHO	Piperidine + pyridine	Steam bath	4-HO-2-CH ₃ C ₆ H ₃ CH=CHCO ₂ H (60)	1135
2-HO-3-CH ₃ OC ₆ H ₃ CHO	Aniline	Room, then boiling C ₂ H ₅ OH	2-HO-3-CH ₃ OC ₆ H ₃ CH=CHCO ₂ H (Quant.)	147, 448
3-HO-4-CH ₃ OC ₆ H ₃ CHO	Piperidine + pyridine	100°, then boil	3-HO-4-CH ₃ OC ₆ H ₃ CH=CHCO ₂ H (Excellent)	449
3-HO-5-CH ₃ OC ₆ H ₃ CHO	Piperidine	Boil	3-HO-5-CH ₃ OC ₆ H ₃ CH=CHCO ₂ H (—)	450
4-HO-3-CH ₃ OC ₆ H ₃ CHO (vanillin)	Alcoholic NH ₃	Water bath	4-HO-3-CH ₃ OC ₆ H ₃ CH=CHCO ₂ H (50)	409
	Quinoline	85°	4-HO-3-CH ₃ OC ₆ H ₃ CH=CHCO ₂ H (50)	259
	Pyridine	Water bath	4-HO-3-CH ₃ OC ₆ H ₃ CH=CHCO ₂ H (57)	291
	Piperidine + pyridine	Room	4-HO-3-CH ₃ OC ₆ H ₃ CH=CHCO ₂ H (85)	270, 373, 414
	Aniline + pyridine	55°	4-HO-3-CH ₃ OC ₆ H ₃ CH=CHCO ₂ H (86)	80
	CH ₃ CO ₂ NH ₄	Boiling n-C ₄ H ₉ OH	4-HO-3-CH ₃ OC ₆ H ₃ CH=C(CO ₂ H) ₂ (40)	385
2,4-Dihydroxy-3-methylbenzaldehyde	Aniline + pyridine	40–45°	2,4-Dihydroxy-3-methylbenzaldehyde (92)	451
2,6-Dihydroxy-4-methylbenzaldehyde	Aniline + pyridine	55°	2,6-Dihydroxy-4-methylbenzaldehyde (75)	452
3,4-Dihydroxy-5-methoxybenzaldehyde	Aniline + pyridine	(—)	3,4-Dihydroxy-5-methoxybenzaldehyde (51)	453
4-Methylsulfonylbenzaldehyde	Piperidine + pyridine	Water bath	4-CH ₃ O ₂ SC ₆ H ₄ CH=CHCO ₂ H (77)	454

Note: References 285 to 1153 are on pp. 582–599.

TABLE I—Continued
CONDENSATIONS WITH MALONIC ACID

D. Aromatic Aldehydes or Ketones—Continued				
Aldehyde or Ketone	Catalyst	Temperature	Product(s) and Yield(s) (%)	Refs.
2,3-(HO) ₂ -4-CH ₃ OC ₆ H ₄ CHO	Aniline	Boiling C ₂ H ₅ OH	2,3-(HO) ₂ -4-CH ₃ OC ₆ H ₄ CH=CHCO ₂ H ^a (—)	455
2-Amino-3-methoxybenzaldehyde	Pyridine	" "	 (—)	85
2-Amino-5-methoxybenzaldehyde	"	" "	 (—)	113
Benzene-1,3,5-tricarboxaldehyde	Piperidine + pyridine	Water bath, then reflux	C ₆ H ₃ (CH=CHCO ₂ H) ₃ -1,3,5 (—)	407
5-Chloro-2-methoxyisophthalaldehyde	" "	70°–90°	 (80)	456
2-Acetoxybenzaldehyde	Pyridine	100°	2-CH ₃ CO ₂ C ₆ H ₄ CH=CHCO ₂ H (28)	457
4-Methoxyisophthalaldehyde	Piperidine + pyridine	Steam bath, then boil	 (75)	458
2-Hydroxy-5-methylisophthalaldehyde (mono Schiff base)	Pyridine	—	 (—)	425
4-Carboxymethoxybenzaldehyde	Piperidine + pyridine	Steam bath, then reflux	4-HO ₂ CCH ₂ OC ₆ H ₄ CH=CHCO ₂ H (—)	459
2-Methoxy-3,4-methylenedioxybenzaldehyde	" "	Water bath	2-CH ₃ O-3,4-CH ₂ O ₂ C ₆ H ₂ CH=CHCO ₂ H (—)	460
2,3-Dibromo-4,5-dimethoxybenzaldehyde	—	—	2,3-Br ₂ -4,5-(CH ₃ O) ₂ C ₆ H ₂ CH=CHCO ₂ H (70)	461
3-Bromo-2-nitro-4,5-dimethoxybenzaldehyde	Piperidine + pyridine	Water bath	3-Br-2-O ₂ N-4,5-(CH ₃ O) ₂ C ₆ H ₂ CH=CHCO ₂ H (65)	461
2-Bromo-6-nitro-4,5-dimethoxybenzaldehyde	" "	" "	2-Br-6-O ₂ N-4,5-(CH ₃ O) ₂ C ₆ H ₂ CH=CHCO ₂ H (57)	461
3-Chloro-2-nitro-4,5-dimethoxybenzaldehyde	—	—	3-Cl-2-O ₂ N-4,5-(CH ₃ O) ₂ C ₆ H ₂ CH=CHCO ₂ H (35)	461
3-Iodo-2-nitro-4,5-dimethoxybenzaldehyde	—	—	3-I-2-O ₂ N-4,5-(CH ₃ O) ₂ C ₆ H ₂ CH=CHCO ₂ H (—)	461
3-Bromo-4-ethoxybenzaldehyde	Piperidine + pyridine	100°	3-Br-4-C ₂ H ₅ OC ₆ H ₄ CH=CHCO ₂ H (—)	423
2-Bromo-4,5-dimethoxybenzaldehyde	" "	—	2-Br-4,5-(CH ₃ O) ₂ C ₆ H ₂ CH=CHCO ₂ H (63)	461
3-Bromo-4,5-dimethoxybenzaldehyde	Piperidine + pyridine	Water bath	3-Br-4,5-(CH ₃ O) ₂ C ₆ H ₂ CH=CHCO ₂ H (90)	461, 462
3-Chloro-4-ethoxybenzaldehyde	" "	100°	3-Cl-4-C ₂ H ₅ OC ₆ H ₄ CH=CHCO ₂ H (—)	423
2-Chloro-4,5-dimethoxybenzaldehyde	—	—	2-Cl-4,5-(CH ₃ O) ₂ C ₆ H ₂ CH=CHCO ₂ H (50)	461
3-Chloro-4,5-dimethoxybenzaldehyde	Piperidine + pyridine	Steam bath, then boil; or room	3-Cl-4,5-(CH ₃ O) ₂ C ₆ H ₂ CH=CHCO ₂ H (Quant.)	461, 463
3-Iodo-4,5-dimethoxybenzaldehyde	" "	Water bath	3-I-4,5-(CH ₃ O) ₂ C ₆ H ₂ CH=CHCO ₂ H (50)	461, 464
4-CH ₃ CONHC ₆ H ₄ CHO	" "	85°	4-CH ₃ CONHC ₆ H ₄ CH=CHCO ₂ H (92)	465
2-Nitro-4,5-dimethoxybenzaldehyde	" "	100°	2-O ₂ N-4,5-(CH ₃ O) ₂ C ₆ H ₂ CH=CHCO ₂ H (65)	404, 461, 466, 1138
3-Nitro-4,5-dimethoxybenzaldehyde	" "	Water bath	3-O ₂ N-4,5-(CH ₃ O) ₂ C ₆ H ₂ CH=CHCO ₂ H (74)	372
2-C ₂ H ₅ C ₆ H ₄ CHO	" "	60°, then 105°	2-C ₂ H ₅ C ₆ H ₄ CH=CHCO ₂ H (—)	429
4-C ₂ H ₅ C ₆ H ₄ CHO	" "	Water bath	4-C ₂ H ₅ C ₆ H ₄ CH=CHCO ₂ H (81)	359
3,4-(CH ₃) ₂ C ₆ H ₃ CHO	Pyridine or pyridine + piperidine	Steam bath	3,4-(CH ₃) ₂ C ₆ H ₃ CH=CHCO ₂ H (72)	467, 468
2-C ₂ H ₅ OC ₆ H ₄ CHO	Pyridine	Water bath	2-C ₂ H ₅ OC ₆ H ₄ CH=CHCO ₂ H (99)	444, 469
	None	" "	2-C ₂ H ₅ OC ₆ H ₄ CH=C(CO ₂ H) ₂ (68)	469
3-C ₂ H ₅ OC ₆ H ₄ CHO	Pyridine	Boiling C ₂ H ₅ OH	3-C ₂ H ₅ OC ₆ H ₄ CH=CHCO ₂ H (93)	377
4-C ₂ H ₅ OC ₆ H ₄ CHO	Pyridine or piperidine + pyridine	Steam bath	4-C ₂ H ₅ OC ₆ H ₄ CH=CHCO ₂ H (90–100)	440, 444

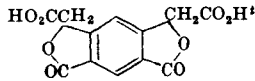
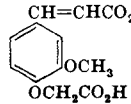
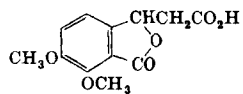
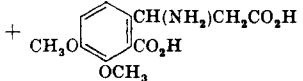
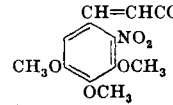
Note: References 285 to 1153 are on pp. 582–599.

^a This product was obtained after hydrolysis of the initially formed coumarin.

TABLE I—Continued
CONDENSATIONS WITH MALONIC ACID

296

ORGANIC REACTIONS

D. Aromatic Aldehydes or Ketones—Continued					
Aldehyde or Ketone	Catalyst	Temperature	Product(s) and Yield(s) (%)	Refs.	
2-Methoxy-4-methylbenzaldehyde	Pyridine	Boiling C ₂ H ₅ OH	2-CH ₃ O-4-CH ₃ C ₆ H ₃ CH=CHCO ₂ H (80)	470	
2-Methoxy-5-methylbenzaldehyde	"	"	2-CH ₃ O-5-CH ₃ C ₆ H ₃ CH=CHCO ₂ H (80)	470	
4-Hydroxy-2,5-dimethylbenzaldehyde	Piperidine + pyridine	100°	4-HO-2,5-(CH ₃) ₂ C ₆ H ₂ CH=CHCO ₂ H (—)	471	
2,3-(CH ₃ O) ₂ C ₆ H ₃ CHO	"	Reflux	2,3-(CH ₃ O) ₂ C ₆ H ₃ CH=CHCO ₂ H (87–98)	271, 472, 473	
2,4-(CH ₃ O) ₂ C ₆ H ₃ CHO	"	Water bath	2,4-(CH ₃ O) ₂ C ₆ H ₃ CH=CHCO ₂ H (98)	412, 474	
	Piperidine	—	2,4-(CH ₃ O) ₂ C ₆ H ₃ CH=CHCO ₂ H (—)	475	
	Pyridine	Boiling C ₂ H ₅ OH	2,4-(CH ₃ O) ₂ C ₆ H ₃ CH=CHCO ₂ H (85)	470	
3,4-(CH ₃ O) ₂ C ₆ H ₃ CHO (veratraldehyde)	Piperidine + pyridine	Steam bath	3,4-(CH ₃ O) ₂ C ₆ H ₃ CH=CHCO ₂ H (Quant.)	476, 477	
	"	Room	3,4-(CH ₃ O) ₂ C ₆ H ₃ CH=CHCO ₂ H (94)	373, 414, 461, 472	
	Alcoholic NH ₃	100°	3,4-(CH ₃ O) ₂ C ₆ H ₃ CH=CHCO ₂ H (50)	478, 479	
	Quinoline	85°	3,4-(CH ₃ O) ₂ C ₆ H ₃ CH=C(CO ₂ H) ₂ (8)		
	Pyridine	Boiling C ₆ H ₅ OH	3,4-(CH ₃ O) ₂ C ₆ H ₃ CH=CHCO ₂ H (69)	259	
	CH ₃ CO ₂ NH ₄	Boiling n-C ₄ H ₉ OH	3,4-(CH ₃ O) ₂ C ₆ H ₃ CH=CHCO ₂ H (77)	360	
			3,4-(CH ₃ O) ₂ C ₆ H ₃ CH(NH ₂)CH ₂ CO ₂ H (52)	385	
			3,4-(CH ₃ O) ₂ C ₆ H ₃ CH=CHCO ₂ H (—)		
3-Hydroxy-4-ethoxybenzaldehyde	Piperidine + pyridine	Water bath	3-HO-4-C ₂ H ₅ OC ₆ H ₃ CH=CHCO ₂ H (74)	480	
4-Hydroxy-3,5-dimethoxybenzaldehyde	Aniline + pyridine	60°	4-HO-3,5-(CH ₃ O) ₂ C ₆ H ₂ CH=CHCO ₂ H (80)	481	
4-(CH ₃) ₂ NC ₆ H ₄ CHO	Piperidine + pyridine	B.p. or water bath	4-(CH ₃) ₂ NC ₆ H ₄ CH=CHCO ₂ H (73)	285, 482	
	"	Room	4-(CH ₃) ₂ NC ₆ H ₄ CH=CHCO ₂ H (80)	482	
	Quinoline	85°	4-(CH ₃) ₂ NC ₆ H ₄ CH=CHCO ₂ H (68)	259	
	Pyridine	50–60°, then room	4-(CH ₃) ₂ NC ₆ H ₄ CH=CHCO ₂ H (50)	360	
4-(CH ₃) ₂ NC ₆ H ₄ CH(OC ₂ H ₅) ₂	Piperidine + pyridine	100°, then 140°	4-(CH ₃) ₂ NC ₆ H ₄ CH=CHCO ₂ H (Quant.)	87	
4,6-Dicarboxybenzene-1,3-dicarboxaldehyde	Pyridine	60°, then 98°	 (67)	483	
Indan-5-carboxaldehyde	Piperidine	60°	 (95)	484	
3-Methoxy-4-acetoxybenzaldehyde	Aniline + pyridine	60°	3-CH ₃ O-4-CH ₃ CO ₂ C ₆ H ₃ CH=C ¹⁴ HCO ₂ H ^u (90)	485	
	Piperidine + pyridine	60°	3-CH ₃ O-4-CH ₃ CO ₂ C ₆ H ₃ CH=CHCO ₂ H (60)	486	
3-Methoxy-4-carboxy-methoxybenzaldehyde	"	100°	 (Quant.)	477	
3,4-Dimethoxy-2-carboxybenzaldehyde (opianic acid)	Alcoholic NH ₃	Water bath			
			+  (35)	76, 77	
4,5-Dimethoxy-2-carboxybenzaldehyde	Piperidine + pyridine	Steam bath, then boil	 (—)	75	
4-Acetamido-2-methoxybenzaldehyde	Alcoholic NH ₃	Heat	4-CH ₃ CONH-2-CH ₃ OC ₆ H ₃ CH=CHCO ₂ H (—)	487	
3-Chloro-4-n-propoxybenzaldehyde	Piperidine + pyridine	100°	3-Cl-4-n-C ₃ H ₇ OC ₆ H ₃ CH=CHCO ₂ H (—)	423	
2-Nitro-3,4,5-trimethoxybenzaldehyde	"	B.p.	 (85)	488	
3-n-C ₃ H ₇ C ₆ H ₄ CHO	"	60°, then 105°	3-n-C ₃ H ₇ C ₆ H ₄ CH=CHCO ₂ H (—)	429	

Note: References 285 to 1153 are on pp. 582–599.

[†] This product was isolated after hydration of the crude reaction product.

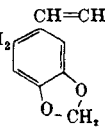
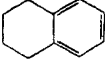
^u The C¹⁴ source was C¹⁴H₃(CO₂H).

THE KNOEVENAGEL CONDENSATION

297

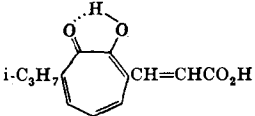
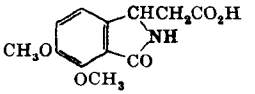
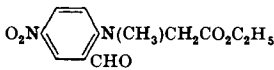
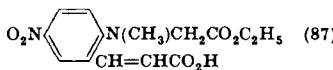
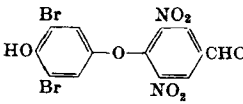
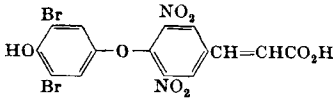
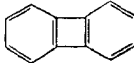
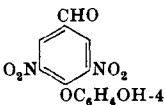
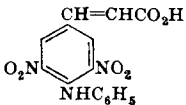
TABLE I—Continued
CONDENSATIONS WITH MALONIC ACID

D. Aromatic Aldehydes or Ketones—Continued

Aldehyde or Ketone	Catalyst	Temperature	Product(s) and Yield(s) (%)	Refs.
4- <i>i</i> -C ₃ H ₇ C ₆ H ₄ CHO	Aniline	Water bath	4-(CH ₃) ₂ CHC ₆ H ₄ CH=CHCO ₂ H (50)	7
	Piperidine + pyridine	" "	4-(CH ₃) ₂ CHC ₆ H ₄ CH=CHCO ₂ H (64)	412
2,3,4-Trimethylbenzaldehyde	Piperidine	100°	2,3,4-(CH ₃) ₃ C ₆ H ₃ CH=CHCO ₂ H (Excellent)	489
2,4,6-Trimethylbenzaldehyde	Piperidine + pyridine	Water bath	2,4,6-(CH ₃) ₃ C ₆ H ₃ CH=CHCO ₂ H (10)	359
2-Isopropoxybenzaldehyde	" "	B.p.	2-(CH ₃) ₂ CHOC ₆ H ₄ CH=CHCO ₂ H (65)	490
3-Isopropoxybenzaldehyde	Pyridine	Water bath	3-(CH ₃) ₂ CHOC ₆ H ₄ CH=CHCO ₂ H (98)	377
4- <i>n</i> -Propoxybenzaldehyde	" "	" "	4- <i>n</i> -C ₃ H ₇ OC ₆ H ₄ CH=CHCO ₂ H (61)	444
	Piperidine + pyridine	100°	4- <i>n</i> -C ₃ H ₇ OC ₆ H ₄ CH=CHCO ₂ H (90–100)	440
4-Methoxy-2,5-dimethylbenzaldehyde	" "	Steam bath	4-CH ₃ O-2,5-(CH ₃) ₂ C ₆ H ₃ CH=CHCO ₂ H (95)	471
2-Methoxy-5-methoxy-methylbenzaldehyde	" "	B.p.	2-CH ₃ O-5-CH ₃ OCH ₂ C ₆ H ₃ CH=CHCO ₂ H (—)	491
3-Methoxy-2-ethoxybenzaldehyde	" "	Water bath, then boil	3-CH ₃ O-2-C ₂ H ₅ OC ₆ H ₃ CH=CHCO ₂ H (Almost quant.)	492
3-Methoxy-4-ethoxybenzaldehyde	" "	Water bath	3-CH ₃ O-4-C ₂ H ₅ OC ₆ H ₃ CH=CHCO ₂ H (89)	412
	Pyridine	—	3-CH ₃ O-4-C ₂ H ₅ OC ₆ H ₃ CH=CHCO ₂ H (90)	493
4-Methoxy-3-ethoxybenzaldehyde	" "	—	4-CH ₃ O-3-C ₂ H ₅ OC ₆ H ₃ CH=CHCO ₂ H (90)	493
	Piperidine + pyridine	Steam bath, then boil	4-CH ₃ O-3-C ₂ H ₅ OC ₆ H ₃ CH=CHCO ₂ H (—)	494
2,6-Dimethoxy-4-methylbenzaldehyde	" "	" "	2,6-(CH ₃ O) ₂ -4-CH ₃ C ₆ H ₃ CH=CHCO ₂ H (98)	495
3,4-Dimethoxy-6-methylbenzaldehyde	" "	Water bath, then boil	3,4-(CH ₃ O) ₂ -6-CH ₃ C ₆ H ₃ CH=CHCO ₂ H (89)	496, 896
2,3,4-Trimethoxybenzaldehyde	" "	" "	2,3,4-(CH ₃ O) ₃ C ₆ H ₃ CH=CHCO ₂ H (94)	412
2,4,5-Trimethoxybenzaldehyde	" "	" "	2,4,5-(CH ₃ O) ₃ C ₆ H ₃ CH=CHCO ₂ H (80)	497, 498
3,4,5-Trimethoxybenzaldehyde	" "	Water bath	3,4,5-(CH ₃ O) ₃ C ₆ H ₃ CH=CHCO ₂ H (80)	412, 499
5-Bromo-8-nitronaphthalene-1-carboxaldehyde	Pyridine	40–45°, then 100°	5-Br-8-O ₂ NC ₁₀ H ₆ CH=CHCO ₂ H-1 (—)	500
5-Bromonaphthalene-1-carboxaldehyde	" "	40–50°, then 100°	5-BrC ₁₀ H ₇ CH=CHCO ₂ H-1 (86)	500
5-Nitronaphthalene-1-carboxaldehyde	" "	B.p.	5-O ₂ NC ₁₀ H ₆ CH=CHCO ₂ H-1 (76)	501
1-Naphthaldehyde	CH ₃ NH ₂ + pyridine	100°, then boil	1-C ₁₀ H ₇ CH=CHCO ₂ H (70)	502, 503
	Pyridine	Steam bath, then boil	1-C ₁₀ H ₇ CH=CHCO ₂ H (60)	504
	CH ₃ CO ₂ NH ₄ /CH ₃ CO ₂ H	Steam bath	1-C ₁₀ H ₇ CH(NH ₂)CH ₂ CO ₂ H (60–74)	505
2-Naphthaldehyde	CH ₃ CO ₂ NH ₄ / in boiling C ₂ H ₅ OH or CH ₃ CO ₂ H on water bath	—	1-C ₁₀ H ₇ CH=CHCO ₂ H (20–26)	506
	CH ₃ NH ₂ Cl + CH ₃ CO ₂ K /CH ₃ CO ₂ H	Water bath	2-C ₁₀ H ₇ CH(NH ₂)CH ₂ CO ₂ H (65–69)	506
	Pyridine	Water bath	2-C ₁₀ H ₇ CH(NHCH ₃)CH ₂ CO ₂ H (56)	506
	Piperidine + pyridine	Steam bath, then boil	2-C ₁₀ H ₇ CH=CHCO ₂ H (39)	504, 507
		Steam bath	2-C ₁₀ H ₇ CH=CHCO ₂ H (<i>trans</i>) (—)	508
2-Hydroxy-1-naphthaldehyde	Aniline	Water bath	2-C ₁₀ H ₇ CH=CHCO ₂ H (90)	508
	Pyridine	100°	2-C ₁₀ H ₇ CH=CHCO ₂ H (72)	81
			2-C ₁₀ H ₇ CH=CHCO ₂ H (92)	509
3,4-Methylenedioxy-6-allylbenzaldehyde	Pyridine + pyridine	Water bath	CH ₂ =CHCH ₂ -  CH=CHCO ₂ H (51)	510
1,3-Dicarbomethoxybenzaldehyde	" "	—	None	474
Ferrocenecarboxaldehyde	" "	B.p.	C ₅ H ₅ FeC ₅ H ₄ CH=CHCO ₂ H (68)	511
5,6,7,8-Tetrahydronaphthalene-2-carboxaldehyde	Pyridine	Steam bath	 CH=CHCO ₂ H (76)	512

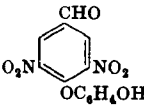

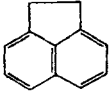


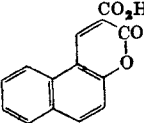
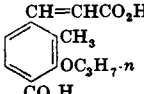
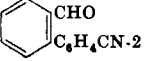
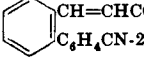
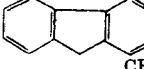

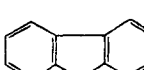
Note: References 285 to 1153 are on pp. 582–599.

TABLE I—Continued
CONDENSATIONS WITH MALONIC ACID

D. Aromatic Aldehydes or Ketones—Continued				
Aldehyde or Ketone	Catalyst	Temperature	Product(s) and Yield(s) (%)	Refs.
7-Isopropyltropolone-3-carboxaldehyde	Pyridine	Water bath	 (85)	416
2-Carbomethoxy-3,4-dimethoxybenzaldehyde (methyl opianate)	Alcoholic NH ₃	B.p.	 (60)	76
	Piperidine + pyridine	Steam bath	2-(CH ₃ O) ₂ C-3,4-(CH ₃ O) ₂ C ₆ H ₂ -CH=CHCO ₂ H (84)	513
3,5-Dimethoxy-4-acetoxybenzaldehyde	Aniline + pyridine	20°, then 50°	3,5-(CH ₃ O) ₂ -4-(CH ₃ CO ₂)C ₆ H ₂ -CH=CHCO ₂ H (84)	514
3-Chloro-4-n-butoxybenzaldehyde	Piperidine + pyridine	100°	3-Cl-4-n-C ₄ H ₉ OC ₆ H ₃ CH=CHCO ₂ H (—)	423
3-Iodo-4-n-butoxybenzaldehyde	" "	100°	3-I-4-n-C ₄ H ₉ OC ₆ H ₃ CH=CHCO ₂ H (—)	423
4-(ClCH ₂ CH ₂) ₂ NC ₆ H ₄ CHO	" "	95°	4-(ClCH ₂ CH ₂) ₂ NC ₆ H ₄ CH=CHCO ₂ H (40)	515
4-n-Butylbenzaldehyde	" "	60°, then 105°	4-n-C ₄ H ₉ C ₆ H ₄ CH=CHCO ₂ H (—)	429
3-CH ₃ -6-i-C ₃ H ₇ C ₆ H ₃ CH(OC ₂ H ₅) ₂	" "	Water bath, then free flame	3-CH ₃ -6-i-C ₃ H ₇ C ₆ H ₃ CH=CHCO ₂ H (35)	516
2-n-Butoxybenzaldehyde	Pyridine	Water bath	2-n-C ₄ H ₉ OC ₆ H ₄ CH=CHCO ₂ H (3)	444
4-n-Butoxybenzaldehyde	" "	Water bath	4-n-C ₄ H ₉ OC ₆ H ₄ CH=CHCO ₂ H (51)	444
	Piperidine + pyridine	100°	4-n-C ₄ H ₉ OC ₆ H ₄ CH=CHCO ₂ H (90-100)	440
2-Hydroxy-6-methyl-3-isopropylbenzaldehyde	Aniline + pyridine	Water bath	2-HO-6-CH ₃ -3-i-C ₃ H ₇ C ₆ H ₃ CH=CHCO ₂ H (—)	83
4-Hydroxy-2-methyl-5-isopropylbenzaldehyde	" "	Water bath	4-HO-2-CH ₃ -5-i-C ₃ H ₇ C ₆ H ₃ CH=CHCO ₂ H (—)	83
4-Hydroxy-3-methoxy-5-n-propylbenzaldehyde	Piperidine + pyridine	Water bath	4-HO-3-CH ₃ O-5-n-C ₃ H ₇ C ₆ H ₂ -CH=CHCO ₂ H (—)	517
2,3-(C ₂ H ₅ O) ₂ C ₆ H ₃ CHO	" "	Water bath, then boil	2,3-(C ₂ H ₅ O) ₂ C ₆ H ₃ CH=CHCO ₂ H (90)	492
3,4-Dimethoxy-6-ethylbenzaldehyde	" "	Steam bath, then boil	3,4-(CH ₃ O) ₂ -6-C ₂ H ₅ C ₆ H ₃ CH=CHCO ₂ H (82)	496
2,3-Dimethoxy-4-ethoxybenzaldehyde	" "	" "	2,3-(CH ₃ O) ₂ -4-C ₂ H ₅ OC ₆ H ₃ CH=CHCO ₂ H (—)	518
2,4-Dimethoxy-3-ethoxybenzaldehyde	" "	" "	2,4-(CH ₃ O) ₂ -3-C ₂ H ₅ OC ₆ H ₃ CH=CHCO ₂ H (57)	518
2,4-Dimethoxy-5-ethoxybenzaldehyde	" "	" "	2,4-(CH ₃ O) ₂ -5-C ₂ H ₅ OC ₆ H ₃ CH=CHCO ₂ H (75)	519, 520
3,4-Dimethoxy-2-ethoxybenzaldehyde	" "	Steam bath	3,4-(CH ₃ O) ₂ -2-C ₂ H ₅ OC ₆ H ₃ CH=CHCO ₂ H (84)	521
3,4-Dimethoxy-6-ethoxybenzaldehyde	" "	100°, then 120°	3,4-(CH ₃ O) ₂ -6-C ₂ H ₅ OC ₆ H ₃ CH=CHCO ₂ H (95)	520
4-Isopropylthio-3-methylbenzaldehyde	" "	Water bath	4-i-C ₃ H ₇ S-3-CH ₃ C ₆ H ₃ CH=CHCO ₂ H (85)	522
4-(C ₂ H ₅) ₂ NC ₆ H ₄ CHO	" "	37°	4-(C ₂ H ₅) ₂ NC ₆ H ₄ CH=CHCO ₂ H (68)	392
5-Chloro-6-methoxy-2-naphthaldehyde	" "	Water bath	5-Cl-6-CH ₃ OC ₁₀ H ₅ CH=CHCO ₂ H-2 (—)	523
	" "	100°	 (87)	1137
3-Chloro-4-n-pentoxybenzaldehyde	" "	100°	3-Cl-4-n-C ₅ H ₁₁ OC ₆ H ₃ CH=CHCO ₂ H (—)	423
2-n-Pentoxybenzaldehyde	Pyridine	100°	2-n-C ₅ H ₁₁ OC ₆ H ₄ CH=CHCO ₂ H (—)	524
4-n-Pentoxybenzaldehyde	Piperidine + pyridine	100°	4-n-C ₅ H ₁₁ OC ₆ H ₄ CH=CHCO ₂ H (90-100)	440
3-Methoxy-2-n-butoxybenzaldehyde	" "	Water bath	3-CH ₃ O-2-n-C ₄ H ₉ OC ₆ H ₃ CH=CHCO ₂ H (68)	480
3-Methoxy-4-n-butoxybenzaldehyde	" "	" "	3-CH ₃ O-4-n-C ₄ H ₉ OC ₆ H ₃ CH=CHCO ₂ H (57)	480
4-Methoxy-3-n-butoxybenzaldehyde	" "	" "	4-CH ₃ O-3-n-C ₄ H ₉ OC ₆ H ₃ CH=CHCO ₂ H (92)	480
3,4-Dimethoxy-2-n-propylbenzaldehyde	" "	Water bath, then boil	3,4-(CH ₃ O) ₂ -2-n-C ₃ H ₇ C ₆ H ₂ -CH=CHCO ₂ H (83)	496
Pentamethoxybenzaldehyde	" "	B.p.	(CH ₃ O) ₅ C ₆ CH=CHCO ₂ H (86)	525
	Pyridine	Steam bath, then boil	 (80)	526
Biphenylene-2-carboxaldehyde	Piperidine + pyridine	Water bath, then boil	 (—)	527
	Aniline + pyridine	Steam bath, then reflux	 (80)	526



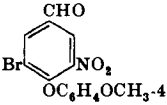
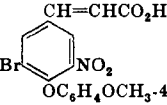
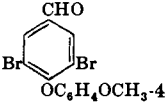

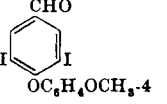
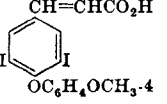
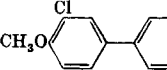
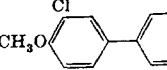
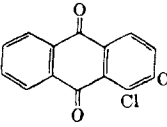
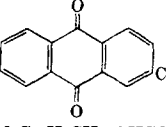
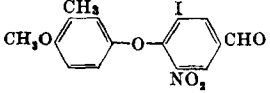
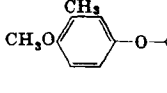
Note: References 285 to 1153 are on pp. 582-599.

TABLE I—Continued
CONDENSATIONS WITH MALONIC ACID

D. Aromatic Aldehydes or Ketones—Continued				
Aldehyde or Ketone	Catalyst	Temperature	Product(s) and Yield(s) (%)	Refs.
 4-(4'-Chlorobenzenesulfonyl)-benzaldehyde 4-(4'-Nitrophenoxy)benzaldehyde 4-(4'-Nitrobenzenesulfonyl)-benzaldehyde Biphenyl-2-carboxaldehyde Biphenyl-4-carboxaldehyde	Pyridine	Steam bath, then boil	 (64)	526
4-(4'-Chlorobenzenesulfonyl)-benzaldehyde	Piperidine + pyridine	100°	4-(4'-ClC6H4SO2)C6H4CH=CHCO2H (67-87)	397
4-(4'-Nitrophenoxy)benzaldehyde	" "	B.p.	4-(4'-O2NC6H4O)C6H4CH=CHCO2H (64)	528
4-(4'-Nitrobenzenesulfonyl)-benzaldehyde	" "	100°	4-(4'-O2NC6H4SO2)C6H4CH=CHCO2H (67-87)	397
Biphenyl-2-carboxaldehyde	Pyridine	Water bath	2-C6H5C6H4CH=CHCO2H (72)	529
Biphenyl-4-carboxaldehyde	"	Boiling C2H5OH	4-C6H5C6H4CH=CHCO2H (54)	350, 530
Acenaphthene-5-carboxaldehyde	"	Steam bath	 (77)	531
2-C6H5OC6H4CHO	Piperidine + pyridine	100°, then boil	2-C6H5OC6H4CH=CHCO2H (100)	532
4-C6H5OC6H4CHO	" "	B.p.	4-C6H5OC6H4CH=CHCO2H (56)	528
4-HOC6H4O  CHO	" "	B.p.	4-HOC6H4O  CH=CHCO2H (67)	528
4-Benzenesulfonylbenzaldehyde	" "	100°	4-C6H5SO2C6H4CH=CHCO2H (67-87)	397
2-Ethoxy-1-naphthaldehyde	Aniline	Water bath	 (71)	82
4-(NCCH2CH2)2NC6H4CHO	Piperidine + pyridine	"	4-(NCCH2CH2)2NC6H4CH=CHCO2H (51)	533
3-Bromo-4-n-hexoxybenzaldehyde	" "	100°	3-Br-4-n-C6H13OC6H4CH=CHCO2H (—)	423
3-Chloro-4-n-hexoxybenzaldehyde	" "	100°	3-Cl-4-n-C6H13OC6H4CH=CHCO2H (—)	423
3-Iodo-4-n-hexoxybenzaldehyde	" "	100°	3-I-4-n-C6H13OC6H4CH=CHCO2H (—)	423
4-n-C6H13OC6H4CHO	" "	100°	4-n-C6H13OC6H4CH=CHCO2H (90-100)	440
3-Methoxy-4-n-pentoxybenzaldehyde	" "	Water bath	3-CH3O-4-n-C6H11OC6H4CH=CHCO2H (91)	534
3-Ethoxy-4-n-butoxybenzaldehyde	" "	" "	3-C2H5O-4-n-C4H9OC6H4CH=CHCO2H (86)	480
3,4-Di-n-propoxybenzaldehyde	" "	" "	3,4-(n-C3H7O)2C6H3CH=CHCO2H (58)	480
3,4-Diisopropoxybenzaldehyde	" "	" "	3,4-(i-C3H7O)2C6H3CH=CHCO2H (37)	480
4-Ethoxy-3-n-propoxy-2-methylbenzaldehyde	" "	Heat	 (Quant.)	535, 536
3,4-Dimethoxy-6-n-butylbenzaldehyde	" "	Water bath, then boil	3,4-(CH2O)2-6-n-C4H9C6H2CH=CHCO2H (95)	496
 C6H4CN-2	" "	80°, then 100°, then boil	 (96)	537
Fluorene-1-carboxaldehyde	" "	Steam bath then 120°	 (97)	538
Fluorene-4-carboxaldehyde	Pyridine	Heat	 (70)	539
Fluorene-9-carboxaldehyde	"	Water bath	 (Small)	132

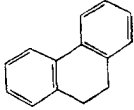
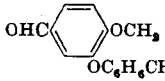
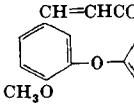
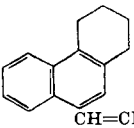
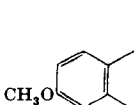
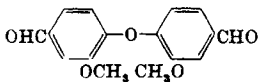

Note: References 285 to 1153 are on pp. 582-599.

TABLE I—Continued
CONDENSATIONS WITH MALONIC ACID

D. Aromatic Aldehydes or Ketones—Continued				
Aldehyde or Ketone	Catalyst	Temperature	Product(s) and Yield(s) (%)	Refs.
 $\text{C}_6\text{H}_5\text{CHO}$	Piperidine + pyridine	95–100°, then 115°	 $\text{C}_6\text{H}_5\text{CH}=\text{CHCO}_2\text{H}$ (97)	540
 $\text{Br}-\text{C}_6\text{H}_3(\text{NO}_2)\text{CHO}$	" "	B.p.	 $\text{Br}-\text{C}_6\text{H}_3(\text{NO}_2)\text{CH}=\text{CHCO}_2\text{H}$ (—)	541
 $\text{Br}-\text{C}_6\text{H}_3(\text{Br})\text{CHO}$	" "	Steam bath	 $\text{Br}-\text{C}_6\text{H}_3(\text{Br})\text{CH}=\text{CHCO}_2\text{H}$ (87)	542
 $\text{I}-\text{C}_6\text{H}_3(\text{I})\text{CHO}$	" "	" "	 $\text{I}-\text{C}_6\text{H}_3(\text{I})\text{CH}=\text{CHCO}_2\text{H}$ (—)	542
 $\text{CH}_3\text{O}-\text{C}_6\text{H}_4\text{CHO}$	" "	B.p.	 $\text{CH}_3\text{O}-\text{C}_6\text{H}_4\text{CH}=\text{CHCO}_2\text{H}$ (70)	528
2-Nitro-5-benzyloxybenzaldehyde	" "	Steam bath, then reflux	2-O ₂ N-5-C ₆ H ₄ CH ₂ OC ₆ H ₅ -CH=CHCO ₂ H (71)	543
4-Benzylbenzaldehyde	Pyridine	Steam bath	4-C ₆ H ₅ CH ₂ C ₆ H ₄ CH=CHCO ₂ H (48)	383
2-Methoxy-5-phenylbenzaldehyde	Piperidine + pyridine	B.p.	2-CH ₃ O-5-C ₆ H ₅ CH ₂ CH=CHCO ₂ H (60)	528
4-Methoxy-3-phenylbenzaldehyde	" "	Steam bath	4-CH ₃ O-3-C ₆ H ₅ CH ₂ CH=CHCO ₂ H (80)	544
2'-Methoxydiphenyl ether-2-carboxaldehyde	" "	" "	2-(2'-CH ₃ OC ₆ H ₄ O)C ₆ H ₄ CH=CHCO ₂ H (—)	532
4'-Methoxydiphenyl ether-4-carboxaldehyde	" "	Heat	4-(4'-CH ₃ OC ₆ H ₄ O)C ₆ H ₄ CH=CHCO ₂ H (88)	545
4-Tosyloxybenzaldehyde	Pyridine	Heat	4-(4'-CH ₃ C ₆ H ₄ SO ₃)C ₆ H ₄ CH=CHCO ₂ H (92)	1136
4-(4'-Methoxybenzenesulfonyl)-benzaldehyde	Piperidine + pyridine	100°	4-(4'-CH ₃ OC ₆ H ₄ SO ₂)C ₆ H ₄ -CH=CHCO ₂ H (67–87)	397
4-N,N-Di-(2'-cyanoethyl)amino-2-methylbenzaldehyde	" "	Water bath	4-(NCCH ₂ CH ₂) ₂ N-2-CH ₃ C ₆ H ₃ -CH=CHCO ₂ H (—)	533
2-Methoxy-5-cyclohexylbenzaldehyde	" "	100°	2-CH ₃ O-5-C ₆ H ₁₁ C ₆ H ₃ CH=CHCO ₂ H (—)	544, 546
4-Methoxy-5-cyclohexylbenzaldehyde	" "	100°	4-CH ₃ O-5-C ₆ H ₁₁ C ₆ H ₃ CH=CHCO ₂ H (—)	544, 546
3-Bromo-4-n-heptoxybenzaldehyde	" "	100°	3-Br-4-n-C ₇ H ₁₅ OC ₆ H ₃ CH=CHCO ₂ H (—)	423
3-Chloro-4-n-heptoxybenzaldehyde	" "	100°	3-Cl-4-n-C ₇ H ₁₅ OC ₆ H ₃ CH=CHCO ₂ H (—)	423
3-Iodo-4-n-heptoxybenzaldehyde	" "	100°	3-I-4-n-C ₇ H ₁₅ OC ₆ H ₃ CH=CHCO ₂ H (—)	423
4-n-Heptoxybenzaldehyde	" "	100°	4-n-C ₇ H ₁₅ OC ₆ H ₄ CH=CHCO ₂ H (90–100)	440
3-Methoxy-4-n-hexoxybenzaldehyde	" "	Water bath	3-CH ₃ O-4-n-C ₆ H ₁₃ OC ₆ H ₃ CH=CHCO ₂ H (96)	480
2,6-Dimethoxy-4-n-pentylbenzaldehyde	" "	Steam bath, then reflux	2,6-(CH ₃ O) ₂ -4-n-C ₅ H ₁₁ C ₆ H ₂ -CH=CHCO ₂ H (86)	495
1-Chloro-9,10-anthraquinone-2-carboxaldehyde	Pyridine	100°	 $\text{CH}=\text{CHCO}_2\text{H}$ (68)	547
9,10-Anthraquinone-2-carboxaldehyde	" "	B.p. or water bath	 $\text{CH}=\text{CHCO}_2\text{H}$ (93)	548, 549, 550
Anthracene-9-carboxaldehyde	Piperidine + pyridine	Steam bath, then reflux	9-C ₁₄ H ₉ CH=CHCO ₂ H (82)	551, 552
Phenanthrene-1-carboxaldehyde	Pyridine	100°	1-C ₁₄ H ₉ CH=CHCO ₂ H (Nearly quant.)	553, 554
Phenanthrene-2-carboxaldehyde	" "	100°	2-C ₁₄ H ₉ CH=CHCO ₂ H (Nearly quant.)	554
Phenanthrene-3-carboxaldehyde	" "	100°	3-C ₁₄ H ₉ CH=CHCO ₂ H (Nearly quant.)	554
Phenanthrene-9-carboxaldehyde	" "	100°	9-C ₁₄ H ₉ CH=CHCO ₂ H (Nearly quant.)	554
 $\text{CH}_3\text{O}-\text{C}_6\text{H}_3(\text{I})(\text{NO}_2)\text{CHO}$	Piperidine + pyridine	B.p.	 $\text{CH}_3\text{O}-\text{C}_6\text{H}_3(\text{I})(\text{NO}_2)\text{CH}=\text{CHCO}_2\text{H}$ (—)	541

Note: References 285 to 1153 are on pp. 582–599.

TABLE I—Continued
CONDENSATIONS WITH MALONIC ACID

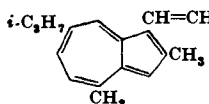
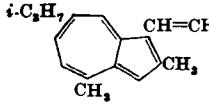
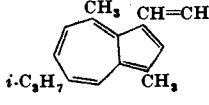
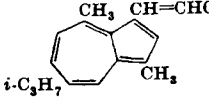
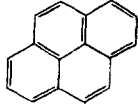
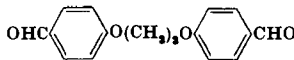
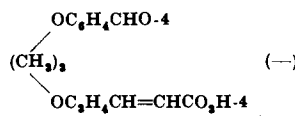
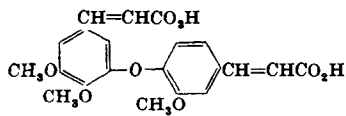
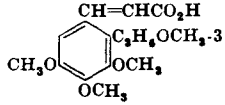
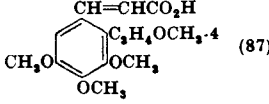
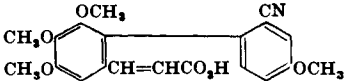
D. Aromatic Aldehydes or Ketones—Continued				
Aldehyde or Ketone	Catalyst	Temperature	Product(s) and Yield(s) (%)	Refs.
Stilbene-4-carboxaldehyde	Pyridine	Boiling C ₂ H ₅ OH or pyridine	4-C ₆ H ₅ CH=CHC ₆ H ₄ CH=CHCO ₂ H (65)	350, 555
	Piperidine + pyridine	B.p.	4-C ₆ H ₅ CH=CHC ₆ H ₄ CH=CHCO ₂ H (70)	556
	Piperidine	Boiling C ₂ H ₅ OH	4-C ₆ H ₅ CH=CHC ₆ H ₄ CH=CHCO ₂ H (65)	557
9,10-Dihydrophenanthrene-2-carboxaldehyde	Piperidine + pyridine	100°, then boil	 CH=CHCO ₂ H (80)	558
4'-Hydroxystilbene-4-carboxaldehyde	" "	B.p.	4-(4'-HOC ₆ H ₄ CH=CH)C ₆ H ₄ CH=CHCO ₂ H (5)	528
	" "	Water bath, then boil	 CH=CHCO ₂ H (94)	559
4-Phenethylbenzaldehyde	" "	B.p.	4-C ₆ H ₅ CH ₂ CH ₂ C ₆ H ₄ CH=CHCO ₂ H (68)	528, 557
1,2,3,4-Tetrahydrophenanthrene-9-carboxaldehyde	Pyridine	—	 CH=CHCO ₂ H (91)	560
3-Methoxy-2-benzyloxybenzaldehyde	Piperidine + pyridine	100°, then boil	3-CH ₃ O-2-C ₆ H ₅ CH ₂ OC ₆ H ₄ CH=CHCO ₂ H (—)	449
3-Methoxy-4-benzyloxybenzaldehyde	" "	Room	3-CH ₃ O-4-C ₆ H ₅ CH ₂ OC ₆ H ₄ CH=CHCO ₂ H (93)	414
	" "	Water bath	3-CH ₃ O-4-C ₆ H ₅ CH ₂ OC ₆ H ₄ CH=CHCO ₂ H (85)	462, 561
4-Methoxy-3-benzylbenzaldehyde	" "	Steam bath	4-CH ₃ O-3-C ₆ H ₅ CH ₂ C ₆ H ₄ CH=CHCO ₂ H (—)	544
3-Bromo-4-n-octyloxybenzaldehyde	" "	100°	3-Br-4-n-C ₈ H ₁₇ OC ₆ H ₄ CH=CHCO ₂ H (—)	423
3-Chloro-4-n-octyloxybenzaldehyde	" "	100°	3-Cl-4-n-C ₈ H ₁₇ OC ₆ H ₄ CH=CHCO ₂ H (—)	423
3-Iodo-4-n-octyloxybenzaldehyde	" "	100°	3-I-4-n-C ₈ H ₁₇ OC ₆ H ₄ CH=CHCO ₂ H (—)	423
4-n-Octyloxybenzaldehyde	" "	100°	4-n-C ₈ H ₁₇ OC ₆ H ₄ CH=CHCO ₂ H (90-100)	440
4-Hydroxy-3,5-di- <i>t</i> -butylbenzaldehyde	" "	Steam bath, then boil	4-HO-3,5-(<i>t</i> -C ₄ H ₉) ₂ C ₆ H ₃ CH=CHCO ₂ H (54)	562
3-Methoxy-4-n-heptoxybenzaldehyde	Aniline	Boiling benzene	4-HO-3,5-(<i>t</i> -C ₄ H ₉) ₂ C ₆ H ₃ CH=CHCO ₂ H (75)	563
3,4-Di- <i>n</i> -butoxybenzaldehyde	Piperidine + pyridine	Water bath	3-CH ₃ O-4-n-C ₄ H ₉ OC ₆ H ₄ CH=CHCO ₂ H (85)	534
3,4-Dimethoxy-6-n-hexylbenzaldehyde	" "	Water bath	3,4-(<i>n</i> -C ₄ H ₉ O) ₂ C ₆ H ₃ CH=CHCO ₂ H (88)	480
	" "	Water bath then boil	3,4-(CH ₃ O) ₂ -6-n-C ₆ H ₁₃ C ₆ H ₂ -CH=CHCO ₂ H (77)	496
7-Methoxy-9,10-dihydrophenanthrene-2-carboxaldehyde	" "	Steam bath, then boil	 CH=CHCO ₂ H (87)	564
4'-Methoxystilbene-4-carboxaldehyde	" "	B.p.	4-(4'-CH ₃ OC ₆ H ₄ CH=CH)C ₆ H ₄ CH=CHCO ₂ H (53)	528
CH ₂ OC ₆ H ₄ CHO-4	" "	140-150°	CH ₂ OC ₆ H ₄ CHO-4 +	565
CH ₂ OC ₆ H ₄ CHO-4	" "		CH ₂ OC ₆ H ₄ CH=CHCO ₂ H-4 +	
	" "		CH ₂ OC ₆ H ₄ CH=CHCO ₂ H-4 (—)	
	" "		CH ₂ OC ₆ H ₄ CH=CHCO ₂ H-4	
	" "	Water bath, then reflux	[HO ₂ CCH=CH ]O (80)	566
2-Methoxy-5-phenethylbenzaldehyde	" "	B.p.	2-CH ₃ O-5-C ₆ H ₅ CH ₂ CH ₂ C ₆ H ₃ -CH=CHCO ₂ H (55)	528
3-Ethoxy-4-benzyloxybenzaldehyde	" "	Water bath	3-C ₂ H ₅ O-4-C ₆ H ₅ CH ₂ OC ₆ H ₄ -CH=CHCO ₂ H (68)	480
2,3,4-Trimethoxybiphenyl-6-carboxaldehyde	" "	100°, then boil	2-C ₆ H ₅ -3,4,5-(CH ₃ O) ₃ C ₆ H ₂ -CH=CHCO ₂ H (—)	567

Note: References 285 to 1153 are on pp. 582-599.

TABLE I—Continued
CONDENSATIONS WITH MALONIC ACID

308

ORGANIC REACTIONS

D. Aromatic Aldehydes or Ketones—Continued					
Aldehyde or Ketone	Catalyst	Temperature	Product(s) and Yield(s) (%)	Refs.	
2,4-Dimethyl-7-isopropylazulene-1-carboxaldehyde	Piperidine + pyridine	Water bath	 (32)	568	
	(C ₃ H ₇) ₃ NH/C ₃ H ₇ OH	Room	 (8)	568	
3,8-Dimethyl-5-isopropylazulene-1-carboxaldehyde	"	"	 (71)	568	
	Piperidine + pyridine	Water bath	 (32)	568	
3-Bromo-4- <i>n</i> -nonoxybenzaldehyde	"	100°	3-Br-4- <i>n</i> -C ₉ H ₁₉ OC ₆ H ₄ CH=CHCO ₂ H (—)	423	
3-Chloro-4- <i>n</i> -nonoxybenzaldehyde	"	100°	3-Cl-4- <i>n</i> -C ₉ H ₁₉ OC ₆ H ₄ CH=CHCO ₂ H (—)	423	
3-Iodo-4- <i>n</i> -nonoxybenzaldehyde	"	100°	3-I-4- <i>n</i> -C ₉ H ₁₉ OC ₆ H ₄ CH=CHCO ₂ H (—)	423	
4- <i>n</i> -Nonoxybenzaldehyde	"	100°	4- <i>n</i> -C ₉ H ₁₉ OC ₆ H ₄ CH=CHCO ₂ H (90-100)	440	
Pyrene-3-carboxaldehyde	"	Steam bath, then 150°	 (76)	569	
	"	140-150°	CH ₂ (CH ₂ OC ₆ H ₄ CH=CHCO ₂ H-4) ₂ (—)	565	
			 (—)		
2,2',3'-Trimethoxydiphenyl ether-4,5'-dicarboxaldehyde	"	Water bath	 (90)	462	
2,3,3',4'-Tetramethoxybiphenyl-6-carboxaldehyde	"	100°, then boil	 (—)	567	
2,3,4,4'-Tetramethoxybiphenyl-6-carboxaldehyde	"	Water bath, then boil	 (87)	570	
3-Bromo-4- <i>n</i> -decyloxybenzaldehyde	"	100°	3-Br-4- <i>n</i> -C ₁₀ H ₂₁ OC ₆ H ₄ CH=CHCO ₂ H (—)	423	
3-Chloro-4- <i>n</i> -decyloxybenzaldehyde	"	100°	3-Cl-4- <i>n</i> -C ₁₀ H ₂₁ OC ₆ H ₄ CH=CHCO ₂ H (—)	423	
3-Iodo-4- <i>n</i> -decyloxybenzaldehyde	"	100°	3-I-4- <i>n</i> -C ₁₀ H ₂₁ OC ₆ H ₄ CH=CHCO ₂ H (—)	423	
4- <i>n</i> -Decyloxybenzaldehyde	"	100°	4- <i>n</i> -C ₁₀ H ₂₁ OC ₆ H ₄ CH=CHCO ₂ H (90-100)	440	
2'-Cyano-2,3,4,4'-tetramethoxybiphenyl-6-carboxaldehyde	"	80°, then 100°, then boil	 (92)	571, 572	

Note: References 285 to 1153 are on pp. 582–599.

THE KNOEVENAGEL CONDENSATION

309

TABLE I—Continued
CONDENSATIONS WITH MALONIC ACID

310

ORGANIC REACTIONS

D. Aromatic Aldehydes or Ketones—Continued				
Aldehyde or Ketone	Catalyst	Temperature	Product(s) and Yield(s) (%)	Refs.
2'-Cyano-4,4',5',6'-tetramethoxy-biphenyl-2-carboxaldehyde	Piperidine + pyridine	B.p.	2-NC-4,5,6-(CH ₃ O) ₃ C ₆ H ₃ CH=CHCO ₂ H (86)	573
	"	140-150°	4-HO ₂ CCH=CHC ₆ H ₄ O(CH ₂) ₄ OC ₆ H ₄ -CH=CHCO ₂ H-4 + 4-HO ₂ CCH=CHC ₆ H ₄ O(CH ₂) ₄ OC ₆ H ₄ CHO-4 (—)	565
3',4',5'-Trimethoxystilbene-4-carboxaldehyde	"	B.p.	4-[3',4',5'-(CH ₃ O) ₃ C ₆ H ₂ CH=CH]C ₆ H ₄ -CH=CHCO ₂ H (78)	528
2,4-Dimethoxy-6-benzyloxy-5-acetylbenzaldehyde	"	100°	 (30)	574
3-Bromo-4-n-dodecyloxybenzaldehyde	"	100°	3-Br-4-n-C ₁₂ H ₂₅ OC ₆ H ₃ CH=CHCO ₂ H (—)	423
3-Chloro-4-n-dodecyloxybenzaldehyde	"	100°	3-Cl-4-n-C ₁₂ H ₂₅ OC ₆ H ₃ CH=CHCO ₂ H (—)	423
3-Iodo-4-n-dodecyloxybenzaldehyde	"	100°	3-I-4-n-C ₁₂ H ₂₅ OC ₆ H ₃ CH=CHCO ₂ H (—)	423
4-n-Dodecyloxybenzaldehyde	"	100°	4-n-C ₁₂ H ₂₅ OC ₆ H ₄ CH=CHCO ₂ H (90-100)	440
3,4-Dibenzoyloxybenzaldehyde	"	80°, then boil	3,4-(C ₆ H ₅ CH ₂ O) ₂ C ₆ H ₂ CH=CHCO ₂ H (95)	561
1,4-Diphenylnaphthalene-2-carboxaldehyde	"	Water bath, then boil	1,4-(C ₆ H ₅) ₂ C ₁₀ H ₆ CH=CHCO ₂ H-2 (85)	575, 576
3-Bromo-4-n-hexadecyloxybenzaldehyde	"	100°	3-Br-4-n-C ₁₆ H ₃₃ OC ₆ H ₃ CH=CHCO ₂ H (—)	423
3-Chloro-4-n-hexadecyloxybenzaldehyde	"	100°	3-Cl-4-n-C ₁₆ H ₃₃ OC ₆ H ₃ CH=CHCO ₂ H (—)	423
3-Iodo-4-n-hexadecyloxybenzaldehyde	"	100°	3-I-4-n-C ₁₆ H ₃₃ OC ₆ H ₃ CH=CHCO ₂ H (—)	423
4-n-Hexadecyloxybenzaldehyde	"	100°	4-n-C ₁₆ H ₃₃ OC ₆ H ₄ CH=CHCO ₂ H (90-100)	440
3-Bromo-4-n-octadecyloxybenzaldehyde	"	100°	3-Br-4-n-C ₁₈ H ₃₇ OC ₆ H ₃ CH=CHCO ₂ H (—)	423
3-Chloro-4-n-octadecyloxybenzaldehyde	"	100°	3-Cl-4-n-C ₁₈ H ₃₇ OC ₆ H ₃ CH=CHCO ₂ H (—)	423
3-Iodo-4-n-octadecyloxybenzaldehyde	"	100°	3-I-4-n-C ₁₈ H ₃₇ OC ₆ H ₃ CH=CHCO ₂ H (—)	423
4-n-Octadecyloxybenzaldehyde	"	100°	4-n-C ₁₈ H ₃₇ OC ₆ H ₄ CH=CHCO ₂ H (90-100)	440
9,10-Diphenylanthracene-2-carboxaldehyde	"	B.p.	9,10-(C ₆ H ₅) ₂ C ₁₄ H ₈ CH=CHCO ₂ H-2 (90-100)	577
9,10-Diphenylanthracene-2-glyoxylic acid	"	B.p.	9,10-(C ₆ H ₅) ₂ C ₁₄ H ₇ COCH=CHCO ₂ H-2 (86-100)	577

E. Heterocyclic Aldehydes or Ketones

4,5-Dichlorothiophene-2-carboxaldehyde	NH ₃ /C ₂ H ₅ OH	B.p.	4,5-Cl ₂ C ₄ HSCH=C(CO ₂ H) ₂ -2 (—)	578
5-Bromoselenophene-2-carboxaldehyde	Piperidine + pyridine	140°	5-BrC ₄ H ₂ SeCH=CHCO ₂ H-2 (65)	579
5-Chlorothiophene-2-carboxaldehyde	"	Steam bath, then boil	5-ClC ₄ H ₂ SCH=CHCO ₂ H-2 (85)	580
5-Nitrothiophene-2-carboxaldehyde	"	"	5-O ₂ NC ₄ H ₂ SCH=CHCO ₂ H-2 (20)	581, 582
2-Nitrothiophene-3-carboxaldehyde	"	B.p.	2-O ₂ NC ₄ H ₂ SCH=CHCO ₂ H-3 (79)	583
4-Nitrothiophene-2-carboxaldehyde	"	B.p.	4-O ₂ NC ₄ H ₂ SCH=CHCO ₂ H-2 (—)	582
5-Nitroselenophene-2-carboxaldehyde	Pyridine	Water bath	5-O ₂ NC ₄ H ₂ SeCH=CHCO ₂ H-2 (54)	584
5-Nitropyrrole-2-carboxaldehyde	"	Heat	5-O ₂ NC ₄ H ₂ NCH=CHCO ₂ H-2 (—)	585
Furfural	Alcoholic NH ₃	Water bath	C ₄ H ₃ OCH=C(CO ₂ H) ₂ -2* (73)	7
	n-Amylamine	"	C ₄ H ₃ OCH=CHCO ₂ H-2 (—)	121
	Alanine	37°	C ₄ H ₃ OCH=C(CO ₂ H) ₂ -2 (—)	48
	"	Warm	C ₄ H ₃ OCH=CHCO ₂ H-2 (—)	48
	Piperidine + pyridine	B.p.	C ₄ H ₃ OCH=CHCO ₂ H-2 (86)	285, 586
	Aniline	Cold	C ₄ H ₃ OCH=C(CO ₂ H) ₂ -2 + C ₆ H ₅ NH-CH=CHCH=C(OH)CH=NC ₆ H ₅ * (—)	587
	Quinoline	85°	C ₄ H ₃ OCH=CHCO ₂ H-2 (66)	259, 588
	Pyridine	Water bath	C ₄ H ₃ OCH=CHCO ₂ H-2 (91)	291, 589, 590
	HOCH ₂ CH ₂ NH ₂ /C ₂ H ₅ OH	Room	C ₄ H ₃ OCH=C(CO ₂ H) ₂ -2 (76)	382
	CH ₃ CO ₂ NH ₄	Boiling C ₂ H ₅ OH	C ₄ H ₃ OCH(NH ₂)CH ₂ CO ₂ H-2 (32)	290, 591

Note: References 285 to 1153 are on pp. 582-599.

* An excess (100%) of malonic acid was used

* Similar compounds were obtained by using other bases.

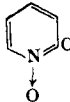
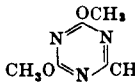
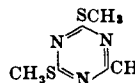
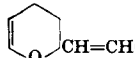
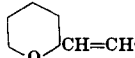
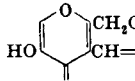
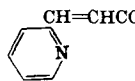
THE KNOEVENAGEL CONDENSATION

311

TABLE I—Continued
CONDENSATIONS WITH MALONIC ACID

312

ORGANIC REACTIONS

E. Heterocyclic Aldehydes or Ketones—Continued				
Aldehyde or Ketone	Catalyst	Temperature	Product(s) and Yield(s) (%)	Refs.
Thiophene-2-carboxaldehyde	Piperidine + pyridine	Water bath, then boil	$C_4H_5SCH=CHCO_2H \cdot 2$ (85) $C_4H_5SCH=CHCO_2H \cdot 2$ (60)	580, 582, 592 392
	" "	37°		
	Alcoholic NH_3 (anhydrous)	70–75°	$C_4H_5SCH=C(CO_2H)_2 \cdot 2$ (85)	593
	Alcoholic NH_3	B.p.	$C_4H_5SCH(NH_3)CH_2CO_2H \cdot 2$ (33) + $C_4H_5SCH=CHCO_2H \cdot 2$ (12)	594
	$CH_3CO_2NH_4$	Boiling C_2H_5OH	$C_4H_5SCH(NH_3)CH_2CO_2H \cdot 2$ (57) + $C_4H_5SCH=CHCO_2H \cdot 2$ (10)	275, 595
Thiophene-3-carboxaldehyde	Pyridine	Water bath	$C_4H_5SCH=CHCO_2H \cdot 3$ (78)	583
	Piperidine + pyridine	Water bath, then boil		
Selenophene-2-carboxaldehyde	Pyridine	100°	$C_4H_5SCH=CHCO_2H \cdot 3$ (85) $C_4H_5SeCH=CHCO_2H \cdot 2$ (75)	596 597
Pyrrole-2-carboxaldehyde	"	Heat	$C_4H_5NHCH=CHCO_2H \cdot 2$ (52)	585
5-Methylimidazole-4-carboxaldehyde	Piperidine	(—)	$5-CH_3C_4H_2N_2CH=C(CO_2H)_2 \cdot 4$ (—)	598
Tetrahydrofuran-2-carboxaldehyde	Piperidine + pyridine	Room, then boil	$C_4H_5OCH=CHCO_2H \cdot 2$ (65)	599
5-Carboxyfuran-2-carboxaldehyde	Pyridine	B.p.	$5-HO_2CC_4H_2OCH=CHCO_2H \cdot 2$ (—)	600
3-Nitropyridine-4-carboxaldehyde*	Piperidine + pyridine	Steam bath	$3-O_2NC_5H_3NCH=CHCO_2H \cdot 4$ (43)	601
Pyridine-3-carboxaldehyde	" "	Water bath	$C_5H_4NCH=CHCO_2H \cdot 3$ (90–95)	234, 602, 603 604
	$CH_3CO_2NH_4$	Boiling C_2H_5OH	$C_5H_4NCH(NH_3)CH_2CO_2H \cdot 3$ + $C_5H_4NCH=CHCO_2H \cdot 3$ (—)	605
Pyridine-2-carboxaldehyde 1-oxide	Pyridine	Water bath	 $CH=CHCO_2H$ (70)	606
5-Methylfuran-2-carboxaldehyde	"	Steam bath	$5-CH_3C_4H_2OCH=CHCO_2H \cdot 2$ (87)	590
5-Hydroxymethylfuran-2-carboxaldehyde	$(C_2H_5)_2NH$	Boiling C_2H_5OH	$5-HOCH_2C_4H_2OCH=C(CO_2H)_2 \cdot 2$ (—)	607
3-Methylthiophene-2-carboxaldehyde	Piperidine + pyridine	Water bath, then boil	$3-CH_3C_4H_2SCH=CHCO_2H \cdot 2$ (80)	580
5-Methylthiophene-2-carboxaldehyde	" "	" "		
	$CH_3CO_2NH_4$	Boiling C_2H_5OH	$5-CH_3C_4H_2SCH=CHCO_2H \cdot 2$ (82) $5-CH_3C_4H_2SCH(NH_3)CH_2CO_2H \cdot 2$ (33) + $5-CH_3C_4H_2SCH=CHCO_2H \cdot 2$ (20)	580 275
5-Methylselenophene-2-carboxaldehyde	Pyridine	Water bath	$5-CH_3C_4H_2SeCH=CHCO_2H \cdot 2$ (60)	608
2,4-Dimethoxy-1,3,5-triazine-6-carboxaldehyde	Piperidine + pyridine	20°, then 100°	 $CH=CHCO_2H$ (25)	609
2,4-Dimethylthio-1,3,5-triazine-6-carboxaldehyde	" "	" "	 $CH=CHCO_2H$ (—)	609
3,4-Dihydro-2H-pyran-2-carboxaldehyde	" "	Room, then b.p.	 $CH=CHCO_2H$ (80)	610
Tetrahydropyran-2-carboxaldehyde	" "	" "	 $CH=CHCO_2H$ (76)	610
3-Hydroxy-6-chloromethyl-γ-pyrone-5-carboxaldehyde	Piperidine/ C_2H_5OH	80°	 $CH=CHCO_2H$ (54)	611
Pyridine-2,6-dicarboxaldehyde	Piperidine + pyridine	Steam bath, then boil	 $CH=CHCO_2H$ (78)	612

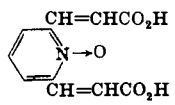
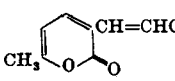
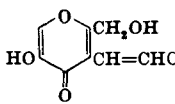
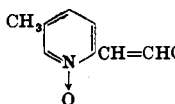
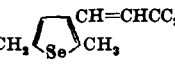
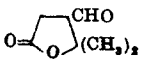
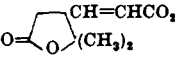
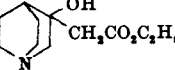
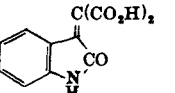
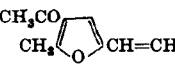
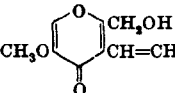
Note: References 285 to 1153 are on pp. 582–599.

* A crude sample of aldehyde was used.

THE KNOEVENAGEL CONDENSATION

313

TABLE I—Continued
CONDENSATIONS WITH MALONIC ACID

E. Heterocyclic Aldehydes or Ketones—Continued				
Aldehyde or Ketone	Catalyst	Temperature	Product(s) and Yield(s) (%)	Refs.
Pyridine-2,6-dicarboxaldehyde 1-oxide	Pyridine	Water bath	 (72)	606
β -2-Furylacrolein	Piperidine + pyridine	30°	$2\text{-C}_4\text{H}_7\text{OCH=CHCH=C(CO}_2\text{H)}_2$ (87)	342
8-Methyl- α -pyrone-3-carboxaldehyde	Piperidine/ $\text{C}_2\text{H}_5\text{OH}$	80°	 (51)	611
5-Carbomethoxyfuran-2-carboxaldehyde	Pyridine	B.p.	$5\text{-CH}_3\text{O}_2\text{CC}_4\text{H}_7\text{OCH=CHCO}_2\text{H}\cdot 2$ (54)	600
3-Hydroxy-6-hydroxymethyl- γ -pyrone-5-carboxaldehyde	Piperidine/ $\text{C}_2\text{H}_5\text{OH}$	80°	 (46)	611
β -2-Thienylacrolein	Piperidine + pyridine	Steam bath	$2\text{-C}_4\text{H}_7\text{SCH=CHCH=C(CO}_2\text{H)}_2$ (82)	342
2-Methylpyridine-3-carboxaldehyde	" "	Water bath	$2\text{-CH}_3\text{C}_5\text{H}_7\text{NCH=CHCO}_2\text{H}\cdot 3$ (50)	613
5-Methylpyridine-2-carboxaldehyde 1-oxide	Pyridine	" "	 (55)	606
5-Ethylthiophene-2-carboxaldehyde	Piperidine + pyridine	Water bath, then boil	$5\text{-C}_2\text{H}_5\text{C}_4\text{H}_7\text{SCH=CHCO}_2\text{H}\cdot 2$ (85)	580
	$\text{CH}_3\text{CO}_2\text{NH}_4$	Boiling alcohol	$5\text{-C}_2\text{H}_5\text{C}_4\text{H}_7\text{SCH=CHCO}_2\text{H}\cdot 2$ (—) + $5\text{-C}_2\text{H}_5\text{C}_4\text{H}_7\text{SCH(NH}_2\text{)CH}_2\text{CO}_2\text{H}\cdot 2$ (30)	275, 595
2,5-Dimethylselenophene-3-carboxaldehyde	Ammonia	(—)	 (31)	1140
	Piperidine + pyridine	Steam bath	 (71)	614
3-Quinuclidone	$\text{CH}_3\text{CO}_2\text{NH}_4$	Boiling benzene	 $\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5$ (40)	615
Isatin	$\text{CH}_3(\text{CO}_2\text{NH}_4)_2/\text{abs. C}_2\text{H}_5\text{OH}$	60°	 $\text{C(CO}_2\text{H)}_2$ (Quant.)	98
5-Methyl-4-acetylfuran-2-carboxaldehyde	Pyridine	Water bath	 (—)	616
3-Methoxy-6-hydroxymethyl- γ -pyrone-5-carboxaldehyde	Piperidine in alcohol	80°	 (46)	611
3-(2'-Pyridyl)propionaldehyde	Piperidine + pyridine	Water bath	$2\text{-C}_4\text{H}_7\text{NCH}_2\text{CH}_2\text{CH=CHCO}_2\text{H}\cdot 2$ (45)	617
5-n-Propylthiophene-2-carboxaldehyde	" "	Water bath, then boil	$5\text{-n-C}_3\text{H}_7\text{C}_4\text{H}_7\text{SCH=CHCO}_2\text{H}\cdot 2$ (83)	580

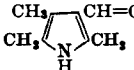
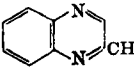
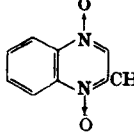
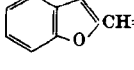
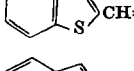
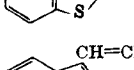
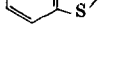
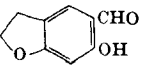
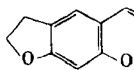
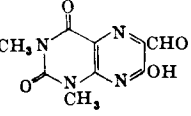
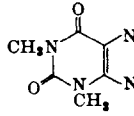
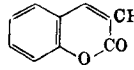
Note: References 285 to 1153 are on pp. 582–599.

* The crude acid obtained was esterified.

TABLE I—Continued
CONDENSATIONS WITH MALONIC ACID

316

ORGANIC REACTIONS

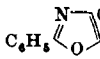
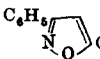
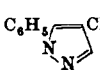
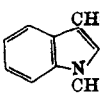
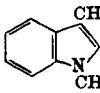
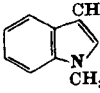
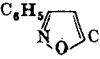
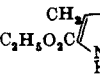
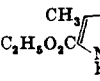
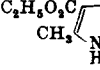


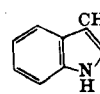
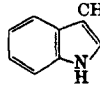
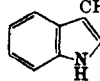
<i>E. Heterocyclic Aldehydes or Ketones—Continued</i>				
Aldehyde or Ketone	Catalyst	Temperature	Product(s) and Yield(s) (%)	Refs.
2,4,5-Trimethylpyrrole-3-carboxaldehyde	Piperidine in alcohol	Water bath	 (—)	618
Quinoxaline-2-carboxaldehyde	Piperidine + pyridine	75°, then boil	 (83)	619
Quinoxaline-2-carboxaldehyde 1,4-bis-oxide	" "	50°, then 80°	 (—)	619
Benzofuran-2-carboxaldehyde	Pyridine	Steam bath	 (80)	620
Benzo[b]thiophene-2-carboxaldehyde	"	Water bath	 (75)	621
	Piperidine + pyridine	Steam bath, then boil	 (81)	622
Benzo[b]thiophene-3-carboxaldehyde	Pyridine	Water bath	 (78)	621
Indole-3-carboxaldehyde	Piperidine + pyridine	38–40°	$C_8H_7NCH=CHCO_2H$ ·3 (50)	623, 624
	Aniline + piperidine	55°	 (94)	625
	Pyridine	Water bath	 (45)	626
4-Carboxy-5-methylfuran-2-carboxaldehyde	" "	" "	$C_5H_4O_3CH=CHCO_2H$ (—)	616
4-Carboxy-5-methylpyrrole-2-carboxaldehyde	Pyridine	Water bath	$4 \cdot C_4H_4O_2C \cdot 5 \cdot CH_3C_4H_2NCH=CHCO_2H \cdot 2$ (—)	616
5-Carboxy-2-methylpyrrole-3-carboxaldehyde	Aniline	Boiling C_2H_5OH	$5 \cdot C_4H_4O_2C \cdot 2 \cdot CH_3C_4H_2NCH=CHCO_2H \cdot 3$ (72)	627
5- <i>t</i> -Butylthiophene-2-carboxaldehyde	$CH_3CO_2NH_4$	" "	$5 \cdot (CH_3)_3CC_4H_2SCH=CHCO_2H \cdot 2$ (—) + $5 \cdot (CH_3)_3CC_4H_2SCH(NH_2)CH_2CO_2H \cdot 2$ (—)	275
2,4-Dimethyl-5-ethylpyrrole-3-carboxaldehyde	Piperidine	" "	$2,4 \cdot (CH_3)_2 \cdot 5 \cdot C_2H_5C_4NHCH=CHCO_2H \cdot 3$ (58)	628
Coumarin-3-carboxaldehyde	Piperidine/ C_2H_5OH	Boiling C_2H_5OH , then heat	 (50–75)	629
4-(4'-Nitrophenyl)thiazole-2-carboxaldehyde	Piperidine + pyridine	Water bath, then 120–125°	$4 \cdot O_2NC_6H_4 \cdot \text{thiazole} \cdot CH=CHCO_2H$ (80)	630
Quinoline-3-carboxaldehyde	" "	Steam bath	$C_8H_6NCH=CHCO_2H \cdot 3$ (80)	392
Quinoline-4-carboxaldehyde	Piperidine/ C_2H_5OH	100°	$C_8H_6NCH=C(CO_2H)_2 \cdot 4$ (80)	42

Note: References 285 to 1153 are on pp. 582–599.

THE KNOEVENAGEL CONDENSATION

317

TABLE I—Continued
CONDENSATIONS WITH MALONIC ACID

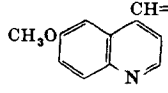
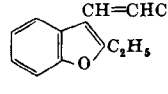
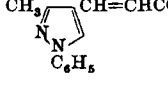
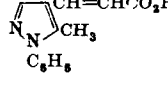
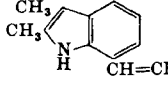
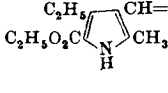
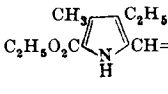
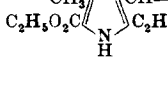
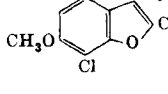
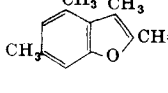
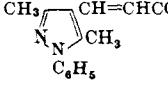
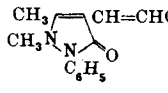
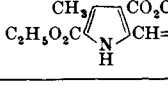
<i>E. Heterocyclic Aldehydes or Ketones—Continued</i>				
Aldehyde or Ketone	Catalyst	Temperature	Product(s) and Yield(s) (%)	Refs.
Quinoline-8-carboxaldehyde	Piperidine + pyridine	Water bath	$C_8H_7NCH=CHCO_2H$ ·8 (83)	631, 632
Isoquinoline-7-carboxaldehyde	Piperidine	Boiling C_2H_5OH	$C_8H_7CH=CHCO_2H$ ·7 (72)	203
2-Phenyloxazole-4-carboxaldehyde	Pyridine	Heat	 $CH=CHCO_2H$ (95)	633
3-Phenylisoxazole-5-carboxaldehyde	„	Water bath	 $CH=CHCO_2H$ (34)	634
1-Phenylpyrazole-4-carboxaldehyde	Piperidine + pyridine	85°, then boil	 $CH=CHCO_2H$ (73)	635
1-Methylindole-3-carboxaldehyde	NH_3/C_2H_5OH	Steam bath	 $CH=C(CO_2H)_2$ (25)*	623
	Piperidine + pyridine	38–40°	 $CH=CHCO_2H$ (7)	623
			 $CH=C(CO_2H)_2$ (30)	
3-Phenyl-4,5-dihydroisoxazole-5-carboxaldehyde	Pyridine	Water bath	 $CH=CHCO_2H$ (50)	634
2,4-Dimethyl-5-carbethoxypyrrole-3-carboxaldehyde	Piperidine	Water bath	 $CH=CHCO_2H$ (Quant.)	636
	Aniline	Boiling C_2H_5OH	 $CH=CHCO_2H$ (68)	637
2,5-Dimethyl-4-carbethoxypyrrole-3-carboxaldehyde	Piperidine	Water bath	 $CH=CHCO_2H$ (95)	618
$(C_2H_5O)_2CH$  CHO	Piperidine + pyridine	Steam bath	$(C_2H_5O)_2CH$  $CH=CHCO_2H$ (76)	638
1-Acetylindole-3-carboxaldehyde	„	80°	 $CH=CHCO_2H^{aa}$ (48)	639
	„	30–40°	 $CH=C(CO_2H)_2^{aa}$ (21)	639
			 $CH=CHCO_2H$ (—)	

Note: References 285 to 1153 are on pp. 582–599.

* Some aldehyde was recovered.

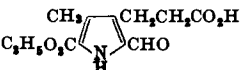
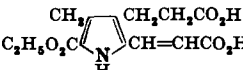
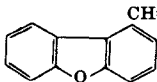
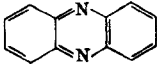
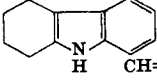
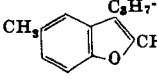
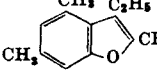
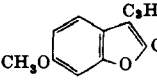
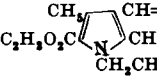
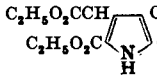
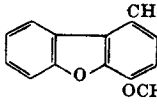
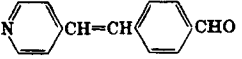
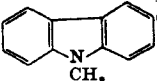
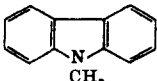
^{aa} The crude product was deacetylated.

TABLE I—Continued
CONDENSATIONS WITH MALONIC ACID

<i>E. Heterocyclic Aldehydes or Ketones—Continued</i>				
Aldehyde or Ketone	Catalyst	Temperature	Product(s) and Yield(s) (%)	Refs.
6-Methoxyquinoline-4-carboxaldehyde	Piperidine + pyridine	Water bath, then boil	 $\text{CH}=\text{CHCO}_2\text{H}$ (65)	227
2-Ethylbenzofuran-3-carboxaldehyde	„ „	Boil	 $\text{CH}=\text{CHCO}_2\text{H}$ (48)	640
3-Methyl-1-phenylpyrazole-4-carboxaldehyde	„ „	100°, then boil	 $\text{CH}=\text{CHCO}_2\text{H}$ (88)	641
5-Methyl-1-phenylpyrazole-4-carboxaldehyde	„ „	100°, then boil	 $\text{CH}=\text{CHCO}_2\text{H}$ (88)	641
2,3-Dimethylindole-7-carboxaldehyde	—	—	 $\text{CH}=\text{CHCO}_2\text{H}$ (—)	642
5-Carbethoxy-2-methyl-4-ethylpyrrole-3-carboxaldehyde	Aniline	Boiling $\text{C}_2\text{H}_5\text{OH}$	 $\text{CH}=\text{CHCO}_2\text{H}$ (—)	644
5-Carbethoxy-4-methyl-3-ethylpyrrole-2-carboxaldehyde	„ „	„ „	 $\text{CH}=\text{CHCO}_2\text{H}$ (95)	643
5-Carbethoxy-4-methyl-2-ethylpyrrole-3-carboxaldehyde	Piperidine	Water bath	 $\text{CH}=\text{CHCO}_2\text{H}$ (—)	645
7-Chloro-4,6-dimethoxy-3-methylbenzofuran-2-carboxaldehyde	Piperidine + pyridine	100°, then 120°	 $\text{CH}=\text{CHCO}_2\text{H}$ (Quant.)	646
3,4,6-Trimethylbenzofuran-2-carboxaldehyde	„ „	100°	 $\text{CH}=\text{CHCO}_2\text{H}$ (—)	647
3,5-Dimethyl-1-phenylpyrazole-4-carboxaldehyde	„ „	100°, then boil	 $\text{CH}=\text{CHCO}_2\text{H}$ (66)	641
1-Phenyl-2,3-dimethyl-5-pyrazolone-4-carboxaldehyde	„ „	130°	 $\text{CH}=\text{CHCO}_2\text{H}$ (45)	648
3,5-Dicarbethoxy-4-methylpyrrole-2-carboxaldehyde	Aniline	Boiling $\text{C}_2\text{H}_5\text{OH}$	 $\text{CH}=\text{CHCO}_2\text{H}$ (50)	649

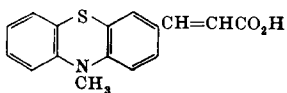
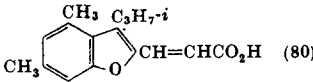
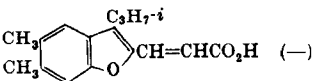
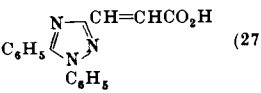
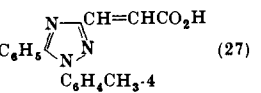
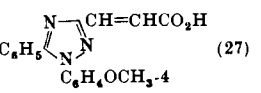
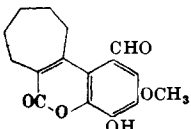
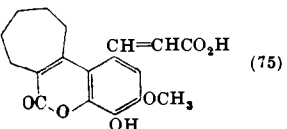
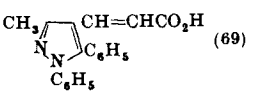
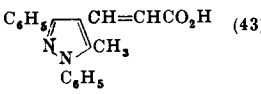
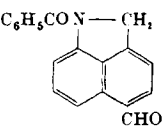
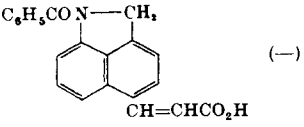
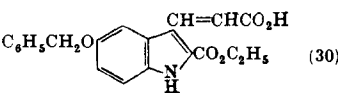
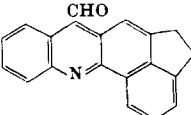
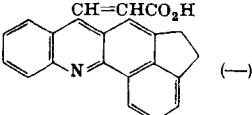
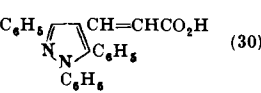
Note: References 285 to 1153 are on pp. 582–599.

TABLE I—Continued
CONDENSATIONS WITH MALONIC ACID

<i>E. Heterocyclic Aldehydes or Ketones—Continued</i>				
Aldehyde or Ketone	Catalyst	Temperature	Product(s) and Yield(s) (%)	Refs.
	Aniline	Boiling C ₂ H ₅ OH	 (60)	627
Dibenzofuran-1-carboxaldehyde	Piperidine + pyridine	Water bath	 (35)	650
Phenazine-2-carboxaldehyde	„ „	Water bath, then boiling point	 CH=CHCO ₂ H (Quant.)	651
1,2,3,4-Tetrahydrocarbazole-8-carboxaldehyde	„ „	Heat	 CH=CHCO ₂ H (50)	652
5-Methyl-3-isopropylbenzofuran-2-carboxaldehyde	„ „	100°	 CH=CHCO ₂ H (—)	653
4,6-Dimethyl-3-ethylbenzofuran-2-carboxaldehyde	„ „	100°	 CH=CHCO ₂ H (—)	647
6-Methoxy-3-isopropylbenzofuran-2-carboxaldehyde	„ „	100°	 CH=CHCO ₂ H (76)	653
5-Carbethoxy-2,4-dimethyl-1-(2'-cyanoethyl)pyrrole-3-carboxaldehyde	Aniline	Boiling C ₂ H ₅ OH	 CH=CHCO ₂ H (95)	654
Ethyl 5-carbethoxy-3-formyl-2-methyl-4-pyrrolacetate	„ „	„ „	 CH=CHCO ₂ H (51)	655
4-Methoxydibenzofuran-1-carboxaldehyde	Pyridine	Steam bath	 CH=CHCO ₂ H (61)	656
	Piperidine + pyridine	100°	4-C ₆ H ₄ NCH=CHC ₆ H ₄ CH=CHCO ₂ H-4 (76)	657
9-Methylcarbazole-3-carboxaldehyde	CH ₃ CO ₂ NH ₄	Boiling C ₂ H ₅ OH	 CH=CHCO ₂ H (55)	591
			 CH(NH ₂)CH ₂ CO ₂ H (28)	

Note: References 285 to 1153 are on pp. 582-599.

TABLE I—Continued
CONDENSATIONS WITH MALONIC ACID

<i>E. Heterocyclic Aldehydes or Ketones—Continued</i>				
Aldehyde or Ketone	Catalyst	Temperature	Product(s) and Yield(s) (%)	Refs.
10-Methylphenothiazine-3-carboxaldehyde	Piperidine + pyridine	90°, then boil	 (86)	658
4,6-Dimethyl-3-isopropylbenzofuran-2-carboxaldehyde	„ „	100°	 (80)	653
5,6-Dimethyl-3-isopropylbenzofuran-2-carboxaldehyde	„ „	100°	 (—)	653
1,5-Diphenyl-1,2,4-triazole-3-carboxaldehyde	„ „	B.p.	 (27)	659, 660
1-p-Tolyl-5-phenyl-1,2,4-triazole-3-carboxaldehyde	„ „	B.p.	 (27)	659, 660
1-Anisyl-5-phenyl-1,2,4-triazole-3-carboxaldehyde	„ „	B.p.	 (27)	659, 660
	Aniline + pyridine	55°	 (75)	661
3-Methyl-1,5-diphenylpyrazole-4-carboxaldehyde	Piperidine + pyridine	100°, then boil	 (69)	641
5-Methyl-1,3-diphenylpyrazole-4-carboxaldehyde	„ „	„	 (43)	641
	Pyridine	Steam bath	 (—)	662
2-Carbethoxy-5-benzyloxyindole-3-carboxaldehyde	„	50–70°	 (30)	1139
	Piperidine + pyridine	100°	 (—)	663
1,3,5-Triphenylpyrazole-4-carboxaldehyde	„ „	100°, then boil	 (30)	641

Note: References 285 to 1153 are on pp. 582–599.

TABLE II
CONDENSATIONS WITH MALONIC ESTERS*

326

ORGANIC REACTIONS

A. Acyclic Aldehydes or Ketones				
Aldehyde or Ketone	Catalyst	Temperature	Product(s) and Yield(s) (%)	Refs.
Formaldehyde	(C ₂ H ₅) ₂ NH or piperidine (C ₂ H ₅) ₂ NH	Room 0°, then water bath	CH ₂ [CH(CO ₂ C ₂ H ₅) ₂] ₂ (—) CH ₂ =C(CO ₂ C ₂ H ₅) ₂ (—) CH ₂ [CH(CO ₂ C ₂ H ₅) ₂] ₂ (—) (C ₂ H ₅ O ₂ C) ₂ C[CH ₂ CH(CO ₂ C ₂ H ₅) ₂] ₂ (—)	1, 2, 664 665, 666
	None	Room, in HCON(CH ₃) ₂	$\left[\begin{array}{c} \text{CO}_2 \\ \diagup \quad \diagdown \\ \text{—CH} \quad \text{C(CH}_3\text{)}_2 \\ \diagdown \quad \diagup \\ \text{CO}_2 \end{array} \right]_2$ (97)	91
Formaldehyde dipiperidide	"	Room	CH ₂ [CH(CO ₂ C ₂ H ₅) ₂] ₂ (—)	2
Formaldehyde (aniline derivative)	"	"	CH ₂ [CH(CO ₂ C ₂ H ₅) ₂] ₂ (40)	2
Acetaldehyde	(C ₂ H ₅) ₂ NH or piperidine †	"	CH ₃ CH[CH(CO ₂ C ₂ H ₅) ₂] ₂ (70) CH ₃ CH=C(CO ₂ C ₂ H ₅) ₂ (25)	2 667
	None	Room, in HCON(CH ₃) ₂	$\left[\begin{array}{c} \text{CO}_2 \\ \diagup \quad \diagdown \\ \text{—CH} \quad \text{C(CH}_3\text{)}_2 \\ \diagdown \quad \diagup \\ \text{CO}_2 \end{array} \right]_2$ (98)	91
Propionaldehyde	Piperidine	Boiling C ₆ H ₆	C ₂ H ₅ CH=C(CO ₂ C ₂ H ₅) ₂ (25)	47
Acetone	Piperidinium acetate	Room	$\begin{array}{c} \text{CO}_2 \\ \diagup \quad \diagdown \\ (\text{CH}_3)_2\text{C}=\text{C} \quad \text{C(CH}_3\text{)}_2 \\ \diagdown \quad \diagup \\ \text{CO}_2 \end{array}$ (13)	91
Crotonaldehyde	Piperidine	Room, then 70° 70–80°	CH ₃ CH=CHCH=C(CO ₂ CH ₃) ₂ (39) CH ₃ CH=CHCH=C(CO ₂ C ₂ H ₅) ₂ (—)	668 669
	(C ₂ H ₅) ₂ NH	Cold	CH ₃ CHCH=CHCH(CO ₂ C ₂ H ₅) ₂ CH(CO ₂ C ₂ H ₅) ₂ (40)	670
	None	Room, in HCON(CH ₃) ₂	CH ₃ CH=CHCH $\left[\begin{array}{c} \text{CO}_2 \\ \diagup \quad \diagdown \\ \text{—CH} \quad \text{C(CH}_3\text{)}_2 \\ \diagdown \quad \diagup \\ \text{CO}_2 \end{array} \right]_2$ (67)	91
2-Methylacrolein†	Piperidinium acetate	Boiling C ₆ H ₆	CH ₂ =C(CH ₃)CH=C(CO ₂ C ₂ H ₅) ₂ (—)	302
n-Butyraldehyde	"	"	n-C ₃ H ₇ CH=C(CO ₂ C ₂ H ₅) ₂ (59)	47
Isobutyraldehyde	(C ₂ H ₅) ₂ NH or piperidine	Room	(CH ₃) ₂ CHCH[CH(CO ₂ C ₂ H ₅) ₂] ₂ (80)	2
	Piperidinium acetate	Boiling C ₆ H ₆	(CH ₃) ₂ CHCH=C(CO ₂ C ₂ H ₅) ₂ (90–92)	47
	Piperidine + CH ₃ CO ₂ H	"	$\begin{array}{c} \text{CO}_2 \\ \diagup \quad \diagdown \\ (\text{CH}_3)_2\text{CHCH}=\text{C} \quad \text{C(CH}_3\text{)}_2 \\ \diagdown \quad \diagup \\ \text{CO}_2 \end{array}$ (81)	671
Dimethyl mesoxalate	Piperidine	Room	(CH ₃ O ₂ C) ₂ C(OH)CH(CO ₂ CH ₃) ₂ (50)	39
n-Valeraldehyde	(C ₂ H ₅) ₂ NH or piperidine	"	n-C ₄ H ₉ CH[CH(CO ₂ C ₂ H ₅) ₂] ₂ (80)	2
	Piperidinium acetate	Boiling C ₆ H ₆	n-C ₄ H ₉ CH=C(CO ₂ C ₂ H ₅) ₂ (44)	47
	Piperidine + pyridine	Steam bath	n-C ₄ H ₉ CH=CHCO ₂ C ₂ H ₅ (78)	672
	Amberlite IR-4B or De-acidite	Boiling C ₆ H ₆	n-C ₄ H ₉ CH=C(CO ₂ C ₂ H ₅) ₂ (33)	181
2-Methylbutyraldehyde	Piperidine + CH ₃ CO ₂ H	"	$\begin{array}{c} \text{CO}_2 \\ \diagup \quad \diagdown \\ \text{C}_2\text{H}_5\text{CH(CH}_3\text{)CH}=\text{C} \quad \text{C(CH}_3\text{)}_2 \\ \diagdown \quad \diagup \\ \text{CO}_2 \end{array}$ (88)	671
3-Methylbutyraldehyde	Piperidinium acetate	"	i-C ₄ H ₉ CH=C(CO ₂ C ₂ H ₅) ₂ (88)	47
	Piperidine	"	i-C ₄ H ₉ CH=C(CO ₂ C ₂ H ₅) ₂ (78)	673
t-C ₄ H ₉ CHO	Piperidine + CH ₃ CO ₂ H	"	$\begin{array}{c} \text{CO}_2 \\ \diagup \quad \diagdown \\ (\text{CH}_3)_3\text{CCH}=\text{C} \quad \text{C(CH}_3\text{)}_2 \\ \diagdown \quad \diagup \\ \text{CO}_2 \end{array}$ (66)	671

Note: References 285 to 1153 are on pp. 582–599.

* The R groups in the malonic ester, CH₂(CO₂R)₂, follow from the structure of the product or are specified in a footnote.







† "Knoevenagel's method" was used for this reaction.

‡ The methylacrolein was added dropwise.

THE KNOEVENAGEL CONDENSATION

327

TABLE II—Continued
CONDENSATIONS WITH MALONIC ESTERS*

A. Acyclic Aldehydes or Ketones—Continued				
Aldehyde or Ketone	Catalyst	Temperature	Product(s) and Yield(s) (%)	Refs.
2-Methyl-2-pentenal	Piperidine	Water bath	$C_2H_5CH=C(CH_3)CH=C(CO_2CH_3)_2$ (35)	668
Hexanal	Piperidinium acetate	Boiling C_6H_6	$n-C_5H_{11}CH=C(CO_2C_2H_5)_2$ (40–46)	47
2-Methylpentanal	"	"	$n-C_5H_{11}CH(CH_3)CH=C(CO_2C_2H_5)_2$ (78)	674
2-Ethylbutanal	"	"	$(C_2H_5)_3CHCH=C(CO_2C_2H_5)_2$ (43–45)	47
Diethyl mesoxalate	Piperidine	Room	$(C_2H_5O_2C)_2C(OH)CH(CO_2C_2H_5)_2$ (50)	39
Heptanal	$(C_2H_5)_2NH$ or piperidine	"	$n-C_6H_{13}CH[CH(CO_2C_2H_5)_2]_2$ (—)	2
	Amberlite IR-4B	—	$n-C_6H_{13}CH=C(CO_2C_2H_5)_2$ (—)	675
	Piperidine + pyridine	Steam bath	$n-C_6H_{13}CH=CHCO_2C_2H_5$ (78)	672
2-Ethylhexanal	Piperidine + caproic acid	Boiling C_6H_6	$n-C_4H_9CH(C_2H_5)CH=C(CO_2C_2H_5)_2$ (87)	69
Citral	Pyridine	100°	"Ethyl citrylideneacetate" (—)	8
	Piperidine	Ice	"Methyl citrylidenemalonate" (63)	668
			$CH_2-CH-CH-CH-CH=C(CO_2C_2H_5)_2$ O O O O (22)	174
2,3,4,5-Diisopropylidene- al-D-arabinose	$(C_2H_5)_2NH/C_6H_5CH_3$	0°	$CH_3-CH_3-CH_3-CH_3$ CH ₃ CH ₃ CH ₃ CH ₃	
cis,trans-Dodeca-5,9-dien- 1,12-dial	Piperidine + pyridine	B.p.	$CH_2CH=CH(CH_2)_3CH=CHCO_2C_2H_5$ $CH_2CH=CHCH_2CH=CHCO_2C_2H_5$ (70)§	676
B. Alicyclic Aldehydes or Ketones				
Cyclopentanone	Aniline chlorozincate	Steam bath	 $=C(CO_2C_2H_5)_2$ (30)	667
Cyclohexanone	"	"	 $=C(CO_2C_2H_5)_2$ (—)	667
Cyclohexene-4-carboxaldehyde	Piperidine	Boiling C_6H_6	 $CH=C(CO_2R)_2$ (—)	677
	"	"	 $CH=CHCO_2CH_3$ (—)	677
	Piperidine + pyridine	Steam bath	 $CH=CHCO_2C_2H_5$ (—)	330
Cyclohexanecarboxaldehyde	Piperidine + CH_3CO_2H	Boiling C_6H_6	 $CH=C \begin{matrix} CO_2 \\ \diagup \quad \diagdown \\ C(CH_3)_2 \end{matrix} \begin{matrix} CO_2 \\ \diagdown \quad \diagup \end{matrix} (63)$	671
C. Aromatic Aldehydes or Ketones				
Phenylacetaldehyde	$(C_2H_5)_2NH$	Room	$C_6H_5CH_2CH(CH_2CO_2H)_2$ ¶ (—)	678
			$C_6H_5CH_2CH=CHCO_2H$ (—)	
Cinnamaldehyde	Piperidine	0° or –12°	$C_6H_5CH=CHCH[CH(CO_2C_2H_5)_2]_2$ (—)	679
	"	Room	$C_6H_5CH=CHCH=C(CO_2C_2H_5)_2$ (—)	680
	None	Room, in $HCON(CH_3)_2$	$C_6H_5CH=CHCH=C \begin{matrix} CO_2 \\ \diagup \quad \diagdown \\ C(CH_3)_2 \end{matrix} \begin{matrix} CO_2 \\ \diagdown \quad \diagup \end{matrix} (75)$	91
	Piperidine + CH_3CO_2H	Boiling C_6H_6	$C_6H_5CH=CHCH=C \begin{matrix} CO_2 \\ \diagup \quad \diagdown \\ C(CH_3)_2 \end{matrix} \begin{matrix} CO_2 \\ \diagdown \quad \diagup \end{matrix} (78)$	671

Note: References 285 to 1153 are on pp. 582–599.

* The R groups in the malonic ester, $CH_2(CO_2R)_2$, follow from the structure of the product or are specified in a footnote.

§ The yield reported was of crude material.

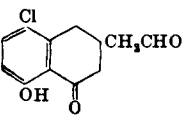
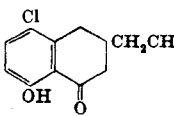
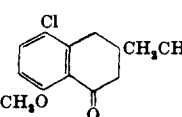
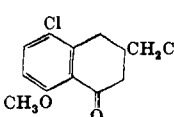
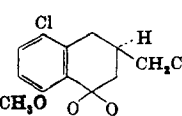
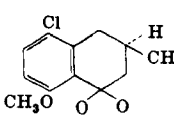
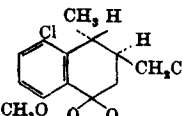
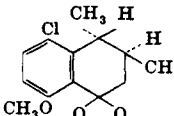
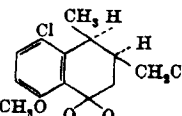
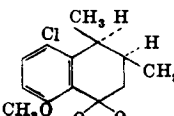
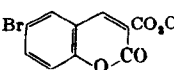
|| Compounds where R = CH_3 , C_2H_5 , $i-C_3H_7$, and $sec-C_4H_9$ were obtained.

¶ This acid was obtained by hydrolysis of the crude product.

TABLE II—Continued
CONDENSATIONS WITH MALONIC ESTERS*

330

ORGANIC REACTIONS

C. Aromatic Aldehydes or Ketones—Continued				
Aldehyde or Ketone	Catalyst	Temperature	Product(s) and Yield(s) (%)	Refs.
$C_6H_5CH=CHCH(OC_2H_5)_2$	Piperidine	Boiling C_6H_6	$C_6H_5CH=CHCH=C(CO_2H)CO_2C_2H_5$ (65)	87
Methyl phenylglyoxylate	NH_3 , CH_3NH_2 , or piperidine	0°	$C_6H_5C(CO_2CH_3)CH(CO_2CH_3)_2$ (80)	37
$C_6H_5CH_2SCH_2CHO$	Piperidine + pyridine	—	$C_6H_5CH_2SCH_2CH=CHCO_2CH_3$ (70)	681
3,4-Methylenedioxybenzaldehyde	Piperidine/ CH_3OH	Room	$3,4-(CH_2O)_2C_6H_3CH=CHCH=C(CO_2CH_3)_2$ (20)	682
2-Methylcinnamaldehyde	Pyridine	Steam bath	$2 \cdot CH_3C_6H_4CH=CHCH=C(CO_2CH_3)_2$ (20)	342
	"	"	$2 \cdot CH_3C_6H_4CH=CHCH=C(CO_2C_2H_5)_2$ (40)	342
5-Phenyl-2,4-pentadienal	Piperidine + CH_3CO_2H	Boiling $CHCl_3$	$C_6H_5CH=CHCH=CHCH=C \begin{array}{c} CO_2 \\ \diagup \quad \diagdown \\ C(CH_3)_2 \end{array} \begin{array}{c} CO_2 \\ \diagdown \quad \diagup \\ C(CH_3)_2 \end{array}$ (32)	671
	Piperidinium acetate	Boiling C_6H_6	 $CH_2CH=C(CO_2R)_2^{**}$ (—)	683
	"	"	 $CH_2CH=C(CO_2C_2H_5)_2$ (—)	683
4-Diethylaminocinnamaldehyde	Piperidine	—	$4 \cdot (C_2H_5)_2NC_6H_4CH=CHCH=C(CO_2C_2H_5)_2$ (—)	684
	Piperidinium acetate	Boiling C_6H_6	 $CH_2CH=C(CO_2CH_3)_2$ (67)	685
3-Cyano-3,3-diphenylpropionaldehyde	Piperidine + $C_6H_5CO_2H$	"	$(C_6H_5)_3C(CN)CH_2CH=C(CO_2C_2H_5)_2$ (—)	353
	Piperidinium acetate	"	 $CH_2CH=C(CO_2CH_3)_2^{\dagger\dagger}$ (82)	686
	"	"	 $CH_2CH=C(CO_2C_2H_5)_2$ (71)	685
D. Aromatic Aldehydes or Ketones				
3,5-Dibromosalicylaldehyde	Piperidine	Room	 $CO_2C_2H_5$ (—)	281

Note: References 285 to 1153 are on pp. 582–599.

* The R groups in the malonic ester, $CH_2(CO_2R)_2$, follow from the structure of the product or are specified in a footnote.

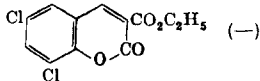
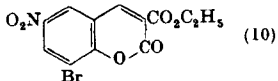
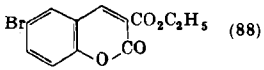
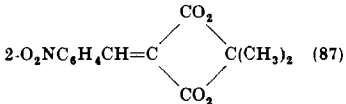
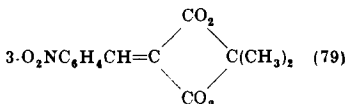
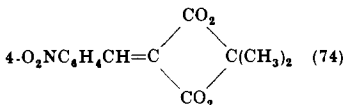
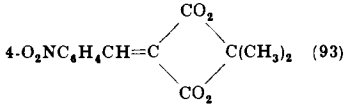
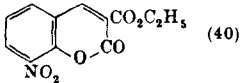
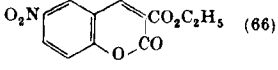
** Diethyl malonate and dibenzyl malonate were used.

†† A mixture of double-bond isomers was obtained.

THE KNOEVENAGEL CONDENSATION

331

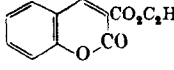
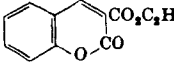
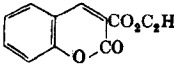
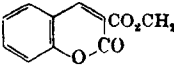
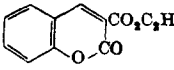
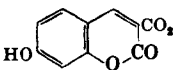
TABLE II—Continued
CONDENSATIONS WITH MALONIC ESTERS*

D. Aromatic Aldehydes or Ketones—Continued				
Aldehyde or Ketone	Catalyst	Temperature	Product(s) and Yield(s) (%)	Refs.
3,5-Dichlorosalicylaldehyde	Piperidine	Room	 (—)	281
3-Bromo-5-nitrosalicylaldehyde	„	Boiling C ₂ H ₅ OH	 (10)	687
2-BrC ₆ H ₄ CHO	Piperidine + C ₆ H ₅ CO ₂ H	Boiling C ₆ H ₆	2-BrC ₆ H ₄ CH=C(CO ₂ C ₂ H ₅) ₂ (88)	155
4-BrC ₆ H ₄ CHO	Piperidine	„	4-BrC ₆ H ₄ CH=C(CO ₂ C ₂ H ₅) ₂ (51)	55
5-Bromosalicylaldehyde	„	Room or boiling C ₂ H ₅ OH	 (88)	281, 687
4-ClC ₆ H ₄ CHO	Pyridine	Water bath	4-ClC ₆ H ₄ CH=C(CO ₂ C ₂ H ₅) ₂ (18)	365
	Piperidine + pyridine	Steam bath	4-ClC ₆ H ₄ CH=CHCO ₂ C ₂ H ₅ (> 75)	93
	Piperidine + n-C ₅ H ₁₁ CO ₂ H	Boiling C ₆ H ₆	4-ClC ₆ H ₄ CH=C(CO ₂ C ₂ H ₅) ₂ (85)	69
2-Nitrobenzaldehyde	Piperidine + CH ₃ CO ₂ H	„	 (87)	671
3-Nitrobenzaldehyde	Piperidine	50–60°	3-O ₂ NC ₆ H ₄ CH=C(CO ₂ C ₂ H ₅) ₂ (—)	688
	Alcoholic NH ₃	Water bath	3-O ₂ NC ₆ H ₄ CH=CHCO ₂ C ₂ H ₅ (70)	92
			3-O ₂ NC ₆ H ₄ CH(NH ₂)CH(CO ₂ C ₂ H ₅) ₂ (29)	
	Piperidine + pyridine	Steam bath	3-O ₂ NC ₆ H ₄ CH=CHCO ₂ CH ₃ (86)	93
	„	„	3-O ₂ NC ₆ H ₄ CH=CHCO ₂ C ₂ H ₅ (85)	93
	Piperidine + CH ₃ CO ₂ H	Boiling CHCl ₃	 (79)	671
4-Nitrobenzaldehyde	Piperidine	50°	4-O ₂ NC ₆ H ₄ CH=C(CO ₂ C ₂ H ₅) ₂ (—)	2
	Piperidine + n-C ₅ H ₁₁ CO ₂ H	Boiling C ₆ H ₆	4-O ₂ NC ₆ H ₄ CH=C(CO ₂ C ₂ H ₅) ₂ (56)	69
	None	Room, (CH ₃) ₂ SO	 (74)	91
	Piperidine + CH ₃ CO ₂ H	Boiling CHCl ₃	 (93)	671
3-Nitrosalicylaldehyde	Piperidine	Boiling C ₂ H ₅ OH	 (40)	687
5-Nitrosalicylaldehyde	„	„	 (66)	687
Benzaldehyde	Piperidine (alone or in C ₂ H ₅ OH)	Room, then water bath	C ₆ H ₅ CH=C(CO ₂ C ₂ H ₅) ₂ (80)	2, 689, 690
	Ethanol NH ₃	Water bath	C ₆ H ₅ CH=CHCO ₂ C ₂ H ₅ (74)	92
			C ₆ H ₅ CH(NH ₂)CH(CO ₂ C ₂ H ₅) ₂ (19)	

Note: References 285 to 1153 are on pp. 582–599.

* The R groups in the malonic ester, CH₂(CO₂R)₂, follow from the structure of the product or are specified in a footnote.

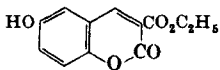
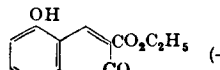
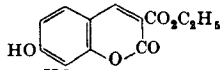
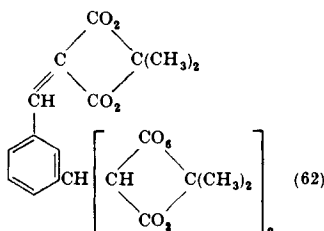
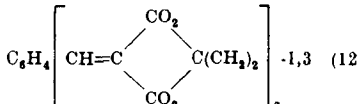
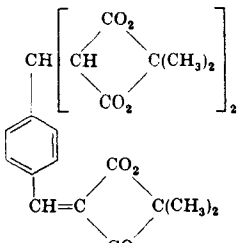
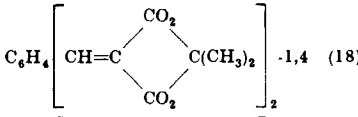
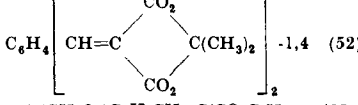
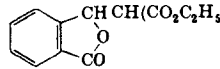
TABLE II—Continued
CONDENSATIONS WITH MALONIC ESTERS*

D. Aromatic Aldehydes and Ketones—Continued				
Aldehyde or ketone	Catalyst	Temperature	Product(s) and Yield(s) (%)	Refs.
Benzaldehyde (contd.)	Piperidine + pyridine	Steam bath	$C_6H_5CH=CHCO_2C_2H_5$ (> 75)	93
	Alcoholic NH_3	Distilled	$C_6H_5CH(NH_2)CH_2CO_2C_2H_5$ (50)	691
	Piperidine	Boiling C_2H_5	$C_6H_5CH=C(CO_2C_2H_5)_2$ (89)	69
	+ $n-C_8H_{17}CO_2H$	—	$C_6H_5CH=C(CO_2C_2H_5)_2$ (60)	675
	Amberlite IR-4B	—		
	None	Room, $(CH_3)_2SO$	$C_6H_5CH=C \begin{array}{c} CO_2 \\ \diagup \quad \diagdown \\ C(CH_3)_2 \end{array}$ (30)	91
			$C_6H_5CH \left[\begin{array}{c} CO_2 \\ \diagup \quad \diagdown \\ -CH \quad C(CH_3)_2 \\ \diagdown \quad \diagup \\ CO_2 \end{array} \right]_2$ (41)	
	"	Room, $HCON(CH_3)_2$	$C_6H_5CH \left[\begin{array}{c} CO_2 \\ \diagup \quad \diagdown \\ -CH \quad C(CH_3)_2 \\ \diagdown \quad \diagup \\ CO_2 \end{array} \right]_2$ (93)	91
	Piperidine + CH_3CO_2H	Boiling C_6H_6	$C_6H_5CH=C \begin{array}{c} CO_2 \\ \diagup \quad \diagdown \\ C(CH_3)_2 \end{array}$ (67)	671
	None	Room, $(CH_3)_2SO$	$C_6H_5CH=C \begin{array}{c} CO_2 \\ \diagup \quad \diagdown \\ CHC_6H_5 \\ \diagdown \quad \diagup \\ CO_2 \end{array}$ (35)	91
Salicylaldehyde	Piperidine or NH_3	Room or boiling C_2H_5OH	 $CO_2C_2H_5$ (80–90)	2, 687
	Piperidine	-10° to -6°	 $CO_2C_2H_5$ (62)	258
	$CH_3NH_2Cl + Na_2CO_3$	—	 $CO_2C_2H_5$ (98)	692
	Piperidine	100°	 $CO_2CH_2CH_2N(C_2H_5)_2$ (Exoellent)	687
	Pyridine	Water bath	 $CO_2C_2H_5$ (58)	1141
3-Hydroxybenzaldehyde	Piperidine + CH_3CO_2H	Boiling $CHCl_3$	$3-HOC_6H_4CH=C \begin{array}{c} CO_2 \\ \diagup \quad \diagdown \\ C(CH_3)_2 \end{array}$ (65)	671
4-Hydroxybenzaldehyde	Piperidine + pyridine	Steam bath or 60°	$4-HOC_6H_4CH=CHCO_2C_2H_5$ (93)	93, 693
	"	60°	$4-HOC_6H_4CH=CHCO_2CH_3$ (87)	693
	Piperidine + CH_3CO_2H	Boiling $CHCl_3$	$4-HOC_6H_4CH=C \begin{array}{c} CO_2 \\ \diagup \quad \diagdown \\ C(CH_3)_2 \end{array}$ (65)	671
2,4-Dihydroxybenzaldehyde	Piperidine	Room	 $CO_2C_2H_5$ (—)	629

Note: References 285 to 1153 are on pp. 582–599.

* The R groups in the malonic ester, $CH_2(CO_2R)_2$, follow from the structure of the product or are specified in a footnote.

TABLE II—Continued
CONDENSATIONS WITH MALONIC ESTERS*

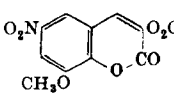
D. Aromatic Aldehydes or Ketones—Continued				
Aldehyde or Ketone	Catalyst	Temperature	Product(s) and Yield(s) (%)	Refs.
2,5-Dihydroxybenzaldehyde	Piperidine	110°	 (70)	694
2,6-Dihydroxybenzaldehyde	„	Room	 (—)	695
3,4-Dihydroxybenzaldehyde (protocatechuic aldehyde)	Piperidine + pyridine	Steam bath	3,4-(HO) ₂ C ₆ H ₃ CH=CHCO ₂ C ₂ H ₅ (90)	93
	„	50°	3,4-(HO) ₂ C ₆ H ₃ CH=CHCO ₂ C ₂ H ₅ (51)	696
	Aniline + piperidine	20°, then 55°	3,4-(HO) ₂ C ₆ H ₃ CH=CHCO ₂ CH ₃ (80)	975
2,3,4-Trihydroxybenzaldehyde	Piperidine	Room	 (—)	629
Isophthalaldehyde	None	Room, HCON(CH ₃) ₂	 (62)	91
	„	Room, (CH ₃) ₂ SO	 -1,3 (12)	91
Terephthalaldehyde	Piperidine/C ₂ H ₅ OH	Heat	C ₆ H ₄ [CH=C(CO ₂ C ₂ H ₅) ₂] ₂ -1,4 (72)	697
	None	Room, HCON(CH ₃) ₂	 (98)§	91
	„	Room, (CH ₃) ₂ SO	 -1,4 (18)	91
	Piperidine + CH ₃ CO ₂ H	Boiling CHCl ₃	 -1,4 (52)	671
3,4-Methylenedioxybenzaldehyde (piperonal)	Alcoholic NH ₃	Water bath	3,4-(CH ₂ O) ₂ C ₆ H ₃ CH=C(CO ₂ C ₂ H ₅) ₂ (83)	92
	Alcoholic CH ₃ NH ₂	„	3,4-(CH ₂ O) ₂ C ₆ H ₃ CH(NH ₂)CH(CO ₂ C ₂ H ₅) ₂ (16)	92
	Piperidine + pyridine		3,4-(CH ₂ O) ₂ C ₆ H ₃ CH=C(CO ₂ C ₂ H ₅) ₂ (50) 3,4-(CH ₂ O) ₂ C ₆ H ₃ CH(NHCH ₃)CH(CO ₂ C ₂ H ₅) ₂ (44) 3,4-(CH ₂ O) ₂ C ₆ H ₃ CH=CHCO ₂ C ₂ H ₅ (90)	975
2-Carboxybenzaldehyde	Alcoholic NH ₃	Steam bath	 (75)	698
	Pyridine	110–115°	Diphthalidylamine (—) 2-(HO ₂ C)C ₆ H ₄ CH=C(CO ₂ C ₂ H ₅) ₂ (66)	698

Note: References 285 to 1153 are on pp. 582–599.

* The R groups in the malonic ester, CH₂(CO₂R)₂, follow from the structure of the product or are specified in a footnote.

§ The yield reported was of crude material.

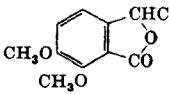
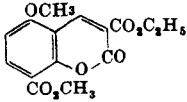
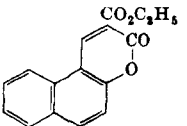
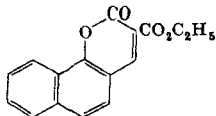
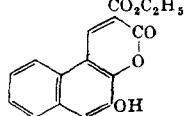
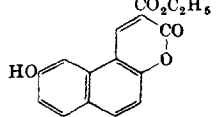
TABLE II—Continued
CONDENSATIONS WITH MALONIC ESTERS*

D. Aromatic Aldehydes or Ketones—Continued				
Aldehyde or Ketone	Catalyst	Temperature	Product(s) and Yield(s) (%)	Refs.
2-Hydroxy-4,5-methylene-dioxybenzaldehyde	Piperidine + pyridine	B.p.	 (81)	419
3-Methoxy-5-nitrosalicylaldehyde	Piperidine	Boiling C ₂ H ₅ OH	 (85)	687
5-Bromovanillin	Piperidine + pyridine	100°	5-Br-4-HO-3-CH ₃ OC ₆ H ₄ CH=CHCO ₂ CH ₃ (87)	723
2-CH ₃ C ₆ H ₄ CHO	Piperidine	—	2-CH ₃ C ₆ H ₄ CH=C(CO ₂ CH ₃) ₂ (—)	668
	Piperidine/C ₆ H ₆	—	2-CH ₃ C ₆ H ₄ CH=C(CO ₂ C ₂ H ₅) ₂ (94)	699
4-CH ₃ C ₆ H ₄ CHO	Piperidine	—	4-CH ₃ C ₆ H ₄ CH=C(CO ₂ C ₂ H ₅) ₂ (58)	700
	Piperidine + pyridine	Steam bath	4-CH ₃ C ₆ H ₄ CH=CHCO ₂ C ₂ H ₅ (>75)	93
4-CH ₃ C ₆ H ₄ CH(OC ₂ H ₅) ₂	None	Boiling C ₆ H ₆	4-CH ₃ C ₆ H ₄ CH=C(CO ₂ H)CO ₂ C ₂ H ₅ (50)	87
2-Methoxybenzaldehyde	Piperidine	Room	2-CH ₃ OC ₆ H ₄ CH=C(CO ₂ C ₂ H ₅) ₂ (—)	2
	Piperidine + CH ₃ CO ₂ H	Boiling C ₆ H ₆	 (79)	671
4-Methoxybenzaldehyde (anisaldehyde)	Piperidine or (C ₂ H ₅) ₂ NH	Room, then water bath	4-CH ₃ OC ₆ H ₄ CH=C(CO ₂ C ₂ H ₅) ₂ (—)	2
	Piperidine + pyridine	Steam bath	4-CH ₃ OC ₆ H ₄ CH=CHCO ₂ C ₂ H ₅ (>75)	93
	Piperidine + <i>n</i> -C ₃ H ₇ CO ₂ H or 4-CH ₃ OC ₆ H ₄ CO ₂ H	Boiling C ₆ H ₆	4-CH ₃ OC ₆ H ₄ CH=C(CO ₂ C ₂ H ₅) ₂ (86)	69, 701
	Piperidine + CH ₃ CO ₂ H	Boiling CHCl ₃	 (72)	671
2-Hydroxy-3-methoxybenzaldehyde	Piperidine	Boiling C ₂ H ₅ OH or room	 (81)	146, 281, 687
4-Hydroxy-3-methoxybenzaldehyde (vanillin)	(C ₂ H ₅) ₂ NH or piperidine	85–90°	4-HO-3-CH ₃ OC ₆ H ₄ CH=C(CO ₂ C ₂ H ₅) ₂ (80)	702
	Pyridine + piperidine + aniline	Room, then 50°	4-HO-3-CH ₃ OC ₆ H ₄ CH=CHCO ₂ C ₂ H ₅ (86)	514
	Piperidine + CH ₃ CO ₂ H	Boiling C ₆ H ₆	 (65)	671
2-Hydroxy-5-hydroxymethylbenzaldehyde	Piperidine + pyridine	Water bath	 (—)	491
2-CH ₃ O ₂ CC ₆ H ₄ CHO	Pyridine	115°	2-HO ₂ CC ₆ H ₄ CH=C(CO ₂ C ₂ H ₅) ₂ (25)	698
2-CH ₃ CO ₂ C ₆ H ₄ CHO	"	105–110°	2-CH ₃ O ₂ CC ₆ H ₄ CH=C(CO ₂ C ₂ H ₅) ₂ (Minor)	457
			2-CH ₃ CO ₂ C ₆ H ₄ CH=C(CO ₂ C ₂ H ₅) ₂ (33)	
2,4-Dihydroxy-3-acetylbenzaldehyde	Piperidine	Room	 (—)	703
2,6-Dihydroxy-3-acetylbenzaldehyde	"	"	 (—)	704
Methyl 2,4-dihydroxy-3-formylbenzoate	Piperidine + pyridine	100°	 (60)	695

Note: References 285 to 1153 are on pp. 582–599.

* The R groups in the malonic ester, CH₂(CO₂R)₂, follow from the structure of the product or are specified in a footnote.

TABLE II—Continued
CONDENSATIONS WITH MALONIC ESTERS*

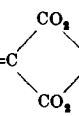
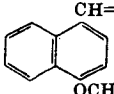
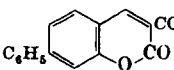
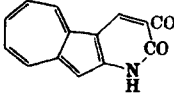
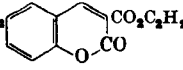
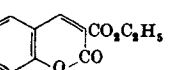
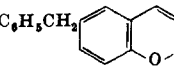
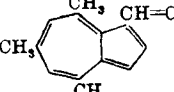
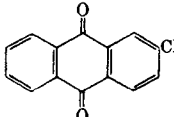
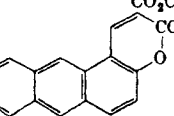
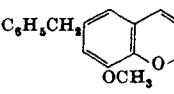
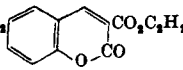
D. Aromatic Aldehydes or Ketones—Continued				
Aldehyde or Ketone	Catalyst	Temperature	Product(s) and Yield(s) (%)	Refs.
3,4-Dimethoxy-6-nitro-benzaldehyde	Piperidine + pyridine	Room	3,4-(CH ₃ O) ₂ C ₆ H ₃ NC ₆ H ₄ CH=C(CO ₂ C ₂ H ₅) ₂ (65)	466
2,5-Dimethoxybenzaldehyde	Piperidine	Steam bath	2,5-(CH ₃ O) ₂ C ₆ H ₃ CH=C(CO ₂ C ₂ H ₅) ₂ (—)	705
3,5-Dimethoxybenzaldehyde	"	Boiling C ₂ H ₅	3,5-(CH ₃ O) ₂ C ₆ H ₃ CH=C(CO ₂ C ₂ H ₅) ₂ (—)	706
3,5-Dimethoxy-4-hydroxy-benzaldehyde	Piperidine or aniline	Room, then 40°	3,5-(CH ₃ O) ₂ -4-HOC ₆ H ₃ CH=CHCO ₂ C ₂ H ₅ (94)	707
4-(CH ₃) ₂ NC ₆ H ₄ CHO	Piperidine	Boiling C ₂ H ₅ OH	4-(CH ₃) ₂ NC ₆ H ₄ CH=C(CO ₂ C ₂ H ₅) ₂ (30)	708
	Piperidine + pyridine	Steam bath	4-(CH ₃) ₂ NC ₆ H ₄ CH=CHCO ₂ CH ₃ (95)	93
	"	"	4-(CH ₃) ₂ NC ₆ H ₄ CH=CHCO ₂ C ₂ H ₅ (95)	93
2,3-Dimethoxy-6-formyl-benzoic acid	Alcoholic NH ₃	Water bath	 (75)	76, 77
Methyl 2-hydroxy-3-formyl-4-methoxybenzoate	Piperidine + pyridine	Reflux, then 100°	 (65)	709
6-Dimethylaminofulvene-2,3-dicarboxaldehyde	Piperidine in C ₂ H ₅ OH or CHCl ₃	Room	(CH ₃) ₂ NCH=C(CH=CHCO ₂ C ₂ H ₅) ₂ (60)	710, 711
	Piperidine in CHCl ₃	"	(CH ₃) ₂ NCH=C(CH=CHO)CH=CHCO ₂ C ₂ H ₅ (—)	710
			(CH ₃) ₂ NCH=C(CH=CHCO ₂ C ₂ H ₅) ₂ (—)	
4-Isopropylbenzaldehyde (cuminal)	Piperidine	Room, then water bath 120°	4-(CH ₃) ₂ CHC ₆ H ₄ CH=C(CO ₂ C ₂ H ₅) ₂ (—)	2
	"		4-(CH ₃) ₂ CHC ₆ H ₄ CH=C(CO ₂ C ₂ H ₅) ₂ (60)	2
2,3,4-(CH ₃) ₃ C ₆ H ₃ CHO	"	Steam bath	2,3,4-(CH ₃) ₃ C ₆ H ₃ CH=C(CO ₂ C ₂ H ₅) ₂ (—)	489
2,4,5-(CH ₃) ₃ C ₆ H ₃ CHO	"	"	2,4,5-(CH ₃) ₃ C ₆ H ₃ CH=C(CO ₂ C ₂ H ₅) ₂ (42)	712
3,4,5-(CH ₃ O) ₃ C ₆ H ₂ CHO	Piperidine + aniline in pyridine	50° or water bath	3,4,5-(CH ₃ O) ₃ C ₆ H ₂ CH=CHCO ₂ C ₂ H ₅ (72)	273, 514
1-Naphthaldehyde	Piperidine + pyridine	Steam bath	1-C ₁₀ H ₇ CH=CHCO ₂ C ₂ H ₅ (> 75)	93
	Piperidine + C ₆ H ₅ CO ₂ H	Boiling C ₆ H ₆	1-C ₁₀ H ₇ CH=C(CO ₂ C ₂ H ₅) ₂ (85)	97
2-Naphthaldehyde	Piperidine	"	2-C ₁₀ H ₇ CH(CO ₂ H)CH ₂ CO ₂ H ⁺⁺ (63)	713
2-Hydroxy-1-naphthaldehyde	"	Water bath	 (90)	81
1-Hydroxy-2-naphthaldehyde	"	80°	 (65)	694
2,3-Dihydroxy-1-naphthaldehyde	"	110°, then 80°	 (55)	694
2,7-Dihydroxy-1-naphthaldehyde	"	80°	 (80)	694
Ferrocenecarboxaldehyde	Piperidine + CH ₃ CO ₂ H	Boiling CH ₂ Cl ₂	C ₅ H ₅ FeC ₅ H ₄ CH=C(CO ₂)C(CH ₃) ₂ (91)	671

Note: References 285 to 1153 are on pp. 582-599.

* The R groups in the malonic ester, CH₂(CO₂R)₂, follow from the structure of the product or are specified in a footnote.

⁺⁺ The crude product was treated with sodium cyanide and then hydrolyzed.

TABLE II—Continued
CONDENSATIONS WITH MALONIC ESTERS*

D. Aromatic Aldehydes or Ketones—Continued				
Aldehyde or Ketone	Catalyst	Temperature	Product(s) and Yield(s) (%)	Refs.
3,5-Dimethoxy-4-acetoxybenzaldehyde	Piperidine + aniline in pyridine	50°	3,5-(CH ₃ O) ₂ -4-CH ₃ CO ₂ C ₆ H ₃ CH=CHCO ₂ C ₆ H ₅ (72)	514
4-Di-(2'-chloroethyl)amino-benzaldehyde	Piperidine/dioxane	Room	4-(ClCH ₂ CH ₂) ₂ NC ₆ H ₄ CH=C(CO ₂ C ₂ H ₅) ₂ (64)	278
	—	—	4-(ClCH ₂ CH ₂) ₂ NC ₆ H ₄ CH=C  C(CH ₃) ₂ (54)	714
4-Methoxynaphthalene-1-carboxaldehyde	Piperidinium acetate	Boiling C ₆ H ₆	 (—)	715
Biphenyl-4-carboxaldehyde	Piperidine/(C ₂ H ₅) ₂ O	Room, then water bath	4-C ₂ H ₅ C ₂ H ₄ CH=C(CO ₂ C ₂ H ₅) ₂ (23)	716
3-Hydroxybiphenyl-4-carboxaldehyde	Piperidine	Water bath	 (60)	694
2-Acetamidoazulene-1-carboxaldehyde	„	50–60°	 (42)	717, 718
4-(NCCH ₂ CH ₂) ₂ NC ₆ H ₄ CHO	„	Water bath	4-(NCCH ₂ CH ₂) ₂ NC ₆ H ₄ CH=C(CO ₂ C ₂ H ₅) ₂ (90)	533
5-(3',4'-Dichlorobenzyl)-salicylaldehyde	„	(—)	3,4-Cl ₂ C ₆ H ₃ CH ₂  (—)	719
5-(4'-Chlorobenzyl)-salicylaldehyde	„	Room	4-ClC ₆ H ₄ CH ₂  (—)	720
4-Benzylbenzaldehyde	„	Room, then steam bath	4-C ₆ H ₅ CH ₂ C ₆ H ₄ CH=C(CO ₂ C ₂ H ₅) ₂ (42)	383
5-Benzylsalicylaldehyde	„	Room	C ₆ H ₅ CH ₂  (90)	720
4,6,8-Trimethylazulene-1-carboxaldehyde	Piperidine/C ₂ H ₅ OH	„	 (66)	1040
Anthraquinone-2-carboxaldehyde	Piperidine	180–190°	 (—)	721
2-Hydroxyanthracene-1-carboxaldehyde	„	Room	 (—)	722
3-Bromo-4-benzyloxy-5-methoxybenzaldehyde	Pyridine	100°	3-Br-4-C ₂ H ₅ CH ₂ O-5-CH ₃ OC ₆ H ₃ CH=CHCO ₂ CH ₃ (82)	723
3-Methoxy-5-benzylsalicylaldehyde	Piperidine	Room	C ₆ H ₅ CH ₂  (—)	720
3,5-Di- <i>t</i> -butyl-4-hydroxybenzaldehyde	Piperidinium acetate	Boiling C ₆ H ₅ CH ₃	3,5-(<i>t</i> -C ₄ H ₉) ₂ -4-HOC ₆ H ₃ CH=CHC(CO ₂ C ₂ H ₅) ₂ (—)	724
5-(4'-Ethylbenzyl)-salicylaldehyde	Piperidine	Room	4-C ₂ H ₅ C ₂ H ₄ CH ₂  (—)	720

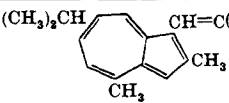
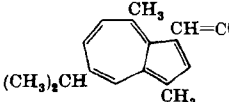
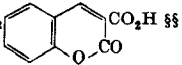
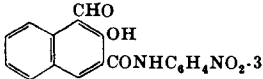
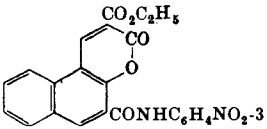
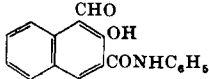
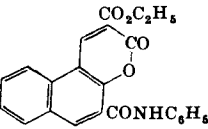
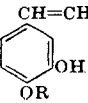
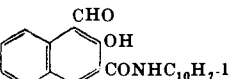
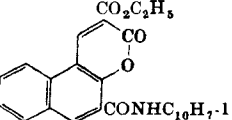
Note: References 285 to 1153 are on pp. 582–599.

*The R groups in the malonic ester, CH₂(CO₂R)₂, follow from the structure of the product or are specified in a footnote.

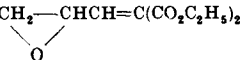
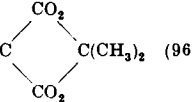
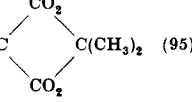
TABLE II—Continued
CONDENSATIONS WITH MALONIC ESTERS*

344

ORGANIC REACTIONS

D. Aromatic Aldehydes or Ketones—Continued				
Aldehyde or Ketone	Catalyst	Temperature	Product(s) and Yield(s) (%)	Refs.
2,4-Dimethyl-7-iso-propylazulene-1-carboxaldehyde	Piperidine/C ₂ H ₅ OH abs.	Room	 (23)	568
3,8-Dimethyl-5-isopropylazulene-1-carboxaldehyde	"	"	 (63)	568
5-(4'-Isopropylbenzyl)salicylaldehyde	Piperidine	"	4-i-C ₃ H ₇ C ₆ H ₄ CH ₂  §§ (—)	720
 Piperidine + pyridine	Water bath		 (—)	725
 "	"	"	 (—)	725
3-Hydroxy-4-tetraacetyl-β-D-glucosyloxybenzaldehyde	Pyridine	55°	 (40)	726
 Piperidine + pyridine	Water bath		 (—)	725

E. Heterocyclic Aldehydes or Ketones

Glycidaldehyde	Piperidinium acetate	Room	 (55)¶¶	175
4,5-Dichlorothiophene-2-carboxaldehyde	Piperidine	18°	4,5-Cl ₂ C ₄ HSCH=C(CO ₂ C ₂ H ₅) ₂ (34)	578
	"	Room	4,5-Cl ₂ C ₄ HSCH=C(CO ₂ C ₂ H ₅) ₂ (62)	578
5-Nitrofurfural	"	Boiling C ₂ H ₅ OH	5-O ₂ NC ₄ H ₂ OCH=C(CO ₂ C ₂ H ₅) ₂ (49)	727
Furfural	Piperidine	Water bath	2-C ₄ H ₃ OCH=C(CO ₂ C ₂ H ₅) ₂ (60)	2
	Piperidine + Pyridine	Steam bath	2-C ₄ H ₃ OCH=CHCO ₂ C ₂ H ₅ (75)	93
	Amberlite IR-4B	—	2-C ₄ H ₃ OCH=C(CO ₂ C ₂ H ₅) ₂ (Poor)	675
	Piperidine + CH ₃ CO ₂ H	Boiling CH ₂ Cl ₂	 (96)	671
Thiophene-2-carboxaldehyde	Piperidine + C ₆ H ₅ CO ₂ H	Boiling C ₆ H ₆	2-C ₄ H ₃ SCH=C(CO ₂ C ₂ H ₅) ₂ (84)	96
	Piperidine + CH ₃ CO ₂ H	Boiling CH ₂ Cl ₂	 (95)	671
Thiophene-3-carboxaldehyde	Pyridine	Water bath	3-C ₄ H ₃ SCH=CHCO ₂ C ₂ H ₅ (86)	583

Note: References 285 to 1153 are on pp. 582-599.

* The R groups in the malonic ester, CH₂(CO₂R)₂, follow from the structure of the product or are specified in a footnote.

§§ The crude product was hydrolyzed.

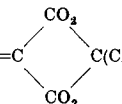
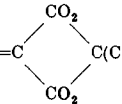





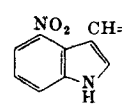
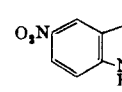
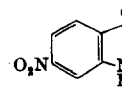

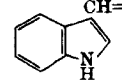
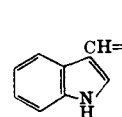
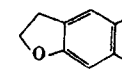
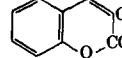
||| R = tetraacetyl-β-D-glucosyl.

¶¶ The yield was calculated on the unrecovered malonate.

THE KNOEVENAGEL CONDENSATION

345

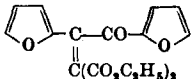
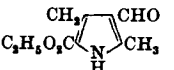
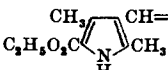


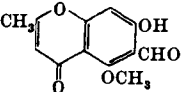
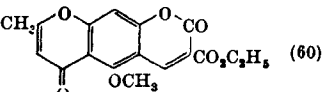
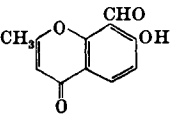
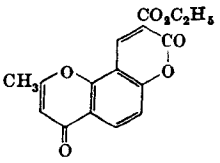
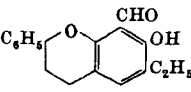
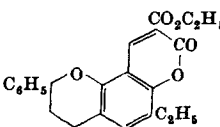
TABLE II—Continued
CONDENSATIONS WITH MALONIC ESTERS*

E. Heterocyclic Aldehydes or Ketones—Continued				
Aldehyde or Ketone	Catalyst	Temperature	Product(s) and Yield(s) (%)	Refs.
Pyrrole-2-carboxaldehyde	Piperidine + CH ₃ CO ₂ H	Boiling CH ₂ Cl ₂	 (76)	671
Pyridine-3-carboxaldehyde	Piperidine	—	3-C ₅ H ₄ NCH=C(CO ₂ C ₂ H ₅) ₂ (73)	168
	Piperidine + CH ₃ CO ₂ H	Boiling CH ₂ Cl ₂	 (35)	671
Pyridine-4-carboxaldehyde hydrochloride	Piperidine + pyridine	Room	4-C ₅ H ₄ NCH=C(CO ₂ C ₂ H ₅) ₂ (62)	728
5-Hydroxymethylfurfural	(C ₂ H ₅) ₂ NH	Steam bath	5-HOCH ₂ C ₄ H ₂ OCH=C(CO ₂ C ₂ H ₅) ₂ -2 (—)	607
4-Methylpyridine-3-carboxaldehyde	Piperidine	Boiling benzene (under N ₂)	 (73)	729
Isatin	(C ₂ H ₅) ₂ NH/C ₂ H ₅ OH	Room	 (57)	98
Ethyl-5-formylpyrrole-2-carboxylate	Piperidine + pyridine	Room	C ₂ H ₅ O ₂ C  CH=C(CO ₂ H)CO ₂ C ₂ H ₅ (80)	730
	„	Water bath	C ₂ H ₅ O ₂ C  CH=CHCO ₂ C ₂ H ₅ (64)	730
Quinuclidine-2-carboxaldehyde	„	Room	 (66)	731
4-Nitroindole-3-carboxaldehyde	„	B.p.	 (70)	732
5-Nitroindole-3-carboxaldehyde	„	B.p.	 (91)	732
6-Nitroindole-3-carboxaldehyde	„	B.p.	 (97)	732
7-Nitroindole-3-carboxaldehyde	„	B.p.	 (95)	732
Indole-3-carboxaldehyde	Piperidinium acetate	Boiling C ₆ H ₆	 (70)	920
	Piperidine + CH ₃ CO ₂ H	Boiling CHCl ₃	 (76)	671
6-Hydroxy-2,3-dihydro-benzofuran-5-carboxaldehyde	Piperidine	Boiling C ₂ H ₅ OH	 (60)	733
Coumarin-3-carboxaldehyde	Piperidine/C ₂ H ₅ OH	Room	 (—)	629

Note: References 285 to 1153 are on pp. 582–599.

* The R groups in the malonic ester, CH₂(CO₂R)₂, follow from the structure of the product or are specified in a footnote.

TABLE II—Continued
CONDENSATIONS WITH MALONIC ESTERS*

E. Heterocyclic Aldehydes or Ketones—Continued				
Aldehyde or Ketone	Catalyst	Temperature	Product(s) and Yield(s) (%)	Refs.
Furil	Piperidine	Boiling C ₂ H ₅ OH	 (—)	734
Quinoline-4-carboxaldehyde hydrate	"	100°	4-C ₁₀ H ₇ NCH=C(CO ₂ C ₂ H ₅) ₂ (57)	42
Quinoline-6-carboxaldehyde	"	—	6-C ₁₀ H ₇ NCH=C(CO ₂ C ₂ H ₅) ₂ (—)	735
	Aniline	Boiling C ₂ H ₅ OH	 (—)	736
(C ₂ H ₅ O) ₂ CH  CHO	Piperidine	100°	(C ₂ H ₅ O) ₂ CH  CH=C(CO ₂ C ₂ H ₅) ₂ (74)	638
		Boiling C ₂ H ₅ OH	 (60)	737
	"	—	 (—)	738
	"	Room	 (—)	739

Note: References 285 to 1153 are on pp. 582–599.

* The R groups in the malonic ester, CH₂(CO₂R)₂, follow from the structure of the product or are specified in a footnote.

TABLE III
CONDENSATIONS WITH SUBSTITUTED MALONIC ACIDS AND ESTERS

The condensations were done at the temperature of the steam bath with piperidine + pyridine as the catalyst unless otherwise stated.

A. Acyclic Aldehyde			
Aldehyde	Acid or Ester	Product(s) and Yield(s) (%)	Refs.
Chloral	$C_2H_5CH(CO_2H)_2$	$CCl_3CHOHCH(C_2H_5)CO_2H$ (—)*	88
	$C_6H_5CH_2CH(CO_2H)_2$	$CCl_3CHOHCH(CH_2C_6H_5)CO_2H$ (—)†	88
B. Aromatic Aldehydes			
2,4- $Cl_2C_6H_3CHO$	$CH_3CH(CO_2H)_2$	2,4- $Cl_2C_6H_3CH=C(CH_3)CO_2H$ (77)	60
2,6- $Cl_2C_6H_3CHO$	$CH_3CH(CO_2H)_2$	2,6- $Cl_2C_6H_3CH=C(CH_3)CO_2H$ (34)	60
3,4- $Cl_2C_6H_3CHO$	$CH_3CH(CO_2H)_2$	3,4- $Cl_2C_6H_3CH=C(CH_3)CO_2H$ (93)	60
4- BrC_6H_4CHO	$CH_3CH(CO_2H)_2$	4- $BrC_6H_4CH=C(CH_3)CO_2H$ (96)	60
2- ClC_6H_4CHO	$CH_3CH(CO_2H)_2$	2- $ClC_6H_4CH=C(CH_3)CO_2H$ (86)	60
3- ClC_6H_4CHO	$CH_3CH(CO_2H)_2$	3- $ClC_6H_4CH=C(CH_3)CO_2H$ (99)	60
4- ClC_6H_4CHO	$CH_3CH(CO_2H)_2$	4- $ClC_6H_4CH=C(CH_3)CO_2H$ (96)	60
2- $O_2NC_6H_4CHO$	$CH_3CH(CO_2H)_2$	2- $O_2NC_6H_4CH=C(CH_3)CO_2H$ (37)	60
3- $O_2NC_6H_4CHO$	$CH_3CH(CO_2H)_2$	3- $O_2NC_6H_4CH=C(CH_3)CO_2H$ (98)	60
	$C_2H_5CH(CO_2H)_2$	3- $O_2NC_6H_4CH=C(C_2H_5)CO_2H$ (64)	60
	$(CH_3)_2CHCH(CO_2H)_2$	None	60
	$CH_2=CHCH_2CH(CO_2H)_2$	3- $O_2NC_6H_4CH=C(CH_2CH=CH_2)CO_2H$ (67)	60
	$n-C_4H_9CH(CO_2H)_2$	3- $O_2NC_6H_4CH=C(C_4H_9-n)CO_2H$ (53)	60
	$n-C_{11}H_{23}CH(CO_2H)_2$	3- $O_2NC_6H_4CH=C(C_{11}H_{23}-n)CO_2H$ (40)	60
4- $O_2NC_6H_4CHO$	$CH_3CH(CO_2H)_2$	4- $O_2NC_6H_4CH=C(CH_3)CO_2H$ (89)	60
	$C_2H_5CH(CO_2H)_2$	4- $O_2NC_6H_4CH=C(C_2H_5)CO_2H$ (60)	60

Note: References 285 to 1153 are on pp. 582-599.

* Pyridine was used as catalyst at water-bath temperature.

† Pyridine was used as catalyst at 60-70°.

TABLE III—Continued
CONDENSATIONS WITH SUBSTITUTED MALONIC ACIDS AND ESTERS

The condensations were done at the temperature of the steam bath with piperidine + pyridine as the catalyst unless otherwise stated.

B. Aromatic Aldehydes—Continued			
Aldehyde	Acid or Ester	Product(s) and Yield(s) (%)	Refs.
C_6H_5CHO	$CH_3CH(CO_2H)_2$	$C_6H_5CHNH_2CH(CH_3)CO_2H$ (60)†	89
	$CH_3CH(CO_2H)_2$	$C_6H_5CH=C(CH_3)CO_2H$ (96)	60
	$CH_3CH(CO_2C_2H_5)_2$	$C_6H_5CHNH_2C(CH_3)(CO_2C_2H_5)_2$ (—)†	89
	$C_2H_5CH(CO_2H)_2$	$C_6H_5CHNH_2CH(C_2H_5)CO_2H$ (28)§	89
	$C_2H_5CH(CO_2H)_2$	$C_6H_5CH=C(C_2H_5)CO_2H$ (60)	60
	$C_2H_5CH(CO_2C_2H_5)_2$	$C_6H_5CHNH_2C(C_2H_5)(CO_2C_2H_5)_2$ (—)†	89
	$C_6H_5CH_2CH(CO_2H)_2$	$C_6H_5CHNH_2CH(CH_2C_6H_5)CO_2H$ (—)§	89
	$CH_3CH(CO_2H)_2$	2- $HOC_6H_4CH=C(CH_3)CO_2H$ (65)	60
2- HOC_6H_4CHO	$CH_3CH(CO_2H)_2$	3- $HOC_6H_4CH=C(CH_3)CO_2H$ (59)	60
3- HOC_6H_4CHO	$CH_3CH(CO_2H)_2$	4- $HOC_6H_4CH=C(CH_3)CO_2H$ (69)	60
4- HOC_6H_4CHO	$CH_3CH(CO_2H)_2$	3,4- $(CH_2O)_2C_6H_3CHNH_2CH(CH_3)CO_2H$ (77)§	89
3,4-Methylenedioxybenzaldehyde (piperonal)	$CH_3CH(CO_2H)_2$	3,4- $(CH_2O)_2C_6H_3CH=C(CH_3)CO_2H$ (79)	60
	$CH_3CH(CO_2C_2H_5)_2$	3,4- $(CH_2O)_2C_6H_3CHNH_2C(CH_3)(CO_2C_2H_5)_2$ (—)	89
	$C_2H_5CH(CO_2H)_2$	3,4- $(CH_2O)_2C_6H_3CHNH_2CH(C_2H_5)CO_2H$ (13)§	89
	$C_2H_5CH(CO_2H)_2$	3,4- $(CH_2O)_2C_6H_3CH=C(C_2H_5)CO_2H$ (30)	60
	$C_2H_5CH(CO_2C_2H_5)_2$	3,4- $(CH_2O)_2C_6H_3CHNH_2C(C_2H_5)(CO_2C_2H_5)_2$ (—)¶	89
	$C_6H_5CH_2CH(CO_2H)_2$	3,4- $(CH_2O)_2C_6H_3CHNH_2CH(CH_2C_6H_5)CO_2H$ (20)‡	89
	$CH_3CH(CO_2H)_2$	2- $CH_3C_6H_4CH=C(CH_3)CO_2H$ (60)	60
	$CH_3CH(CO_2H)_2$	3- $CH_3C_6H_4CH=C(CH_3)CO_2H$ (86)	60
2- $CH_3C_6H_4CHO$	$CH_3CH(CO_2H)_2$	4- $CH_3C_6H_4CH=C(CH_3)CO_2H$ (68)	60
3- $CH_3C_6H_4CHO$	$CH_3CH(CO_2H)_2$	2- $CH_3OC_6H_4CH=C(CH_3)CO_2H$ (85)	60
4- $CH_3C_6H_4CHO$	$CH_3CH(CO_2H)_2$	2- $CH_3OC_6H_4CH=C(C_2H_5)CO_2H$ (55)	60
2- $CH_3OC_6H_4CHO$	$CH_2=CHCH_2CH(CO_2H)_2$	2- $CH_3OC_6H_4CH=C(CH_2CH=CH_2)CO_2H$ (46)	60
	$n-C_4H_9CH(CO_2H)_2$	2- $CH_3OC_6H_4CH=C(C_4H_9-n)CO_2H$ (46)	60
	$n-C_{11}H_{23}CH(CO_2H)_2$	2- $CH_3OC_6H_4CH=C(C_{11}H_{23}-n)CO_2H$ (26)	60

3-CH ₃ OC ₆ H ₄ CHO	CH ₃ CH(CO ₂ H) ₂	3-CH ₃ OC ₆ H ₄ CH=C(CH ₃)CO ₂ H (85)	60
4-CH ₃ OC ₆ H ₄ CHO	CH ₃ CH(CO ₂ H) ₂	4-CH ₃ OC ₆ H ₄ CH=C(CH ₃)CO ₂ H (89)	60
	C ₂ H ₅ CH(CO ₂ H) ₂	4-CH ₃ OC ₆ H ₄ CH=C(C ₂ H ₅)CO ₂ H (43)	60
3-Methoxy-4-hydroxy- benzaldehyde (vanillin)	CH ₃ CH(CO ₂ H) ₂	3-CH ₃ O-4-HOC ₆ H ₃ CH=C(CH ₃)CO ₂ H (34)	60
2,3-(CH ₃ O) ₂ C ₆ H ₃ CHO	CH ₃ CH(CO ₂ H) ₂	2,3-(CH ₃ O) ₂ C ₆ H ₃ CH=C(CH ₃)CO ₂ H (99)	60
3,4-Dimethoxybenz- aldehyde (veratraldehyde)	CH ₃ CH(CO ₂ H) ₂	3,4-(CH ₃ O) ₂ C ₆ H ₃ CH=C(CH ₃)CO ₂ H (91)	60
4-(CH ₃) ₂ NC ₆ H ₄ CHO	CH ₃ CH(CO ₂ H) ₂	4-(CH ₃) ₂ NC ₆ H ₄ CH=C(CH ₃)CO ₂ H (70)	60
2,3-Dimethoxy-6- formylbenzoic acid	C ₂ H ₅ CH(CO ₂ H) ₂	None	60
2,4,6-Trimethyl-3,5- dinitrobenzaldehyde	CH ₃ CH(CO ₂ H) ₂	$\begin{array}{c} \text{CH}=\text{C}(\text{CH}_3)\text{CO}_2\text{H} \\ \text{CH}_3 \quad \quad \quad \text{CH}_3 \\ \text{O}_2\text{N} \quad \quad \quad \text{NO}_2 \end{array}$ (14)	60
4-Isopropylbenzaldehyde	CH ₃ CH(CO ₂ H) ₂	4- <i>i</i> -C ₃ H ₇ C ₆ H ₄ CH=C(CH ₃)CO ₂ H (77)	60
	C ₂ H ₅ CH(CO ₂ H) ₂	4- <i>i</i> -C ₃ H ₇ C ₆ H ₄ CH=C(C ₂ H ₅)CO ₂ H (40)	60
	CH ₂ =CHCH ₂ CH(CO ₂ H) ₂	4- <i>i</i> -C ₃ H ₇ C ₆ H ₄ CH=C(CH ₂ CH=CH ₂)CO ₂ H (24)	60
	<i>n</i> -C ₄ H ₉ CH(CO ₂ H) ₂	4- <i>i</i> -C ₃ H ₇ C ₆ H ₄ CH=C(C ₄ H ₉ - <i>n</i>)CO ₂ H (20)	60
	<i>n</i> -C ₁₁ H ₂₃ CH(CO ₂ H) ₂	None	60
2,4,6-Trimethylbenzaldehyde	CH ₃ CH(CO ₂ H) ₂	None	60
1-Naphthaldehyde	CH ₃ CH(CO ₂ H) ₂	1-C ₁₀ H ₇ CH=C(CH ₃)CO ₂ H (71)	60

C. Heterocyclic Aldehyde

Furfural	CH ₃ CH(CO ₂ H) ₂	2-C ₄ H ₃ OCH=C(CH ₃)CO ₂ H (61)	60
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Note: References 285 to 1153 are on pp. 582-599.

‡ Alcoholic ammonia was used as catalyst at 100°.

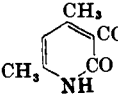
§ Alcoholic ammonia was used as catalyst at 145°.

|| Alcoholic ammonia was used as catalyst at 150°.

¶ Alcoholic ammonia was used as catalyst at 130-140°.

TABLE IV
CONDENSATIONS WITH MALONAMIC ACIDS OR MALONAMIDES

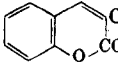
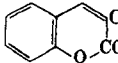
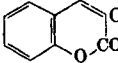
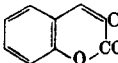
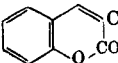
$\begin{array}{c} \text{CONHR} \\ \diagup \quad \diagdown \\ \text{CH}_2 \\ \diagdown \quad \diagup \\ \text{COR}' \end{array}$
 The groups R and R' in CH_2 can be seen from inspection of the structure of the product.

A. Acyclic Aldehydes			
Aldehyde or Ketone	Catalyst/Temperature	Product(s) and Yield(s) (%)	Refs.
$\text{CH}_3\text{CH}_2\text{CHO}$	Piperidine + pyridine/82°	$\text{C}_6\text{H}_5\text{CH}=\text{CHCONH}_2$ (70)	740
$(\text{CH}_3)_2\text{CHCHO}$	Piperidine + pyridine/82°	$(\text{CH}_3)_2\text{CHCH}=\text{CHCONH}_2$ (70)	740
Acetylacetone	$(\text{C}_2\text{H}_5)_2\text{NH}/50^\circ$	 (60)	99
B. Aromatic Aldehyde			
Cinnamaldehyde	Lutidine/—	$\text{C}_6\text{H}_5\text{CH}=\text{CHCH}=\text{C}(\text{CO}_2\text{H})\text{CONHC}_6\text{H}_5$ (53)	741
	Lutidine/—	$\text{C}_6\text{H}_5\text{CH}=\text{CHCH}=\text{C}(\text{CO}_2\text{H})\text{CONHC}_6\text{H}_4\text{CH}_3$ -2 (50)	741
	Lutidine/—	$\text{C}_6\text{H}_5\text{CH}=\text{CHCH}=\text{C}(\text{CO}_2\text{H})\text{CONHC}_6\text{H}_4\text{CH}_3$ -3 (40)	741
	Lutidine/—	$\text{C}_6\text{H}_5\text{CH}=\text{CHCH}=\text{C}(\text{CO}_2\text{H})\text{CONHC}_6\text{H}_4\text{CH}_3$ -4 (37)	741
	Lutidine/—	$\text{C}_6\text{H}_5\text{CH}=\text{CHCH}=\text{C}(\text{CO}_2\text{H})\text{CONHC}_6\text{H}_3(\text{CH}_3)_2$ -3,4 (40)	741
C. Aromatic Aldehydes			
$2,4\text{-Cl}_2\text{C}_6\text{H}_3\text{CHO}$	Piperidine/100°	$2,4\text{-Cl}_2\text{C}_6\text{H}_3\text{CH}=\text{C}(\text{CO}_2\text{H})\text{CONHC}_6\text{H}_4\text{Cl}$ -2 + $2,4\text{-Cl}_2\text{C}_6\text{H}_3\text{CH}=\text{CHCONHC}_6\text{H}_4\text{Cl}$ -2 (—)	742
$3,4\text{-Cl}_2\text{C}_6\text{H}_3\text{CHO}$	Piperidinium acetate/100°	$3,4\text{-Cl}_2\text{C}_6\text{H}_3\text{CH}=\text{C}(\text{CO}_2\text{H})\text{CONHC}_6\text{H}_4\text{Cl}$ -2 + $3,4\text{-Cl}_2\text{C}_6\text{H}_3\text{CH}=\text{CHCONHC}_6\text{H}_4\text{Cl}$ -2 (—)	742
	Piperidinium acetate/100°	$3,4\text{-Cl}_2\text{C}_6\text{H}_3\text{CH}=\text{C}(\text{CO}_2\text{H})\text{CONHC}_6\text{H}_4\text{Cl}$ -3 + $3,4\text{-Cl}_2\text{C}_6\text{H}_3\text{CH}=\text{CHCONHC}_6\text{H}_4\text{Cl}$ -3 (—)	742
	Piperidinium acetate/100°	$3,4\text{-Cl}_2\text{C}_6\text{H}_3\text{CH}=\text{C}(\text{CO}_2\text{H})\text{CONHC}_6\text{H}_4\text{Cl}$ -4 + $3,4\text{-Cl}_2\text{C}_6\text{H}_3\text{CH}=\text{CHCONHC}_6\text{H}_4\text{Cl}$ -4 (—)	742
	Piperidinium acetate/100°	$3,4\text{-Cl}_2\text{C}_6\text{H}_3\text{CH}=\text{C}(\text{CO}_2\text{H})\text{CONHC}_6\text{H}_4\text{Cl}$ -4 + $3,4\text{-Cl}_2\text{C}_6\text{H}_3\text{CH}=\text{CHCONHC}_6\text{H}_4\text{Cl}$ -4 (—)	742
$3,5\text{-Dichloro-2-hydroxybenzaldehyde}$	Pyridine/heat	$3,5\text{-Cl}_2\text{-2HOC}_6\text{H}_3\text{CH}=\text{CHCONHC}_6\text{H}_4\text{I}$ -4 (—)	747
$3\text{-Bromobenzaldehyde}$	Pyridine/100°	$3\text{-BrC}_6\text{H}_4\text{CH}=\text{CHCONHC}_6\text{H}_5$ (99)	101
$2\text{-Chlorobenzaldehyde}$	None/100°	$3\text{-BrC}_6\text{H}_4\text{CH}=\text{C}(\text{CO}_2\text{H})\text{CONHC}_6\text{H}_5$ (72)	101
	Pyridine/100°	$2\text{-ClC}_6\text{H}_4\text{CH}=\text{CHCONHC}_6\text{H}_5$ (70)	101
	None/100°	$2\text{-ClC}_6\text{H}_4\text{CH}=\text{C}(\text{CO}_2\text{H})\text{CONHC}_6\text{H}_5$ (13)	101
	Piperidinium acetate/100°	$2\text{-ClC}_6\text{H}_4\text{CH}=\text{C}(\text{CO}_2\text{H})\text{CONHC}_6\text{H}_5$ (100)	101
$4\text{-Chlorobenzaldehyde}$	Piperidinium acetate/100°	$2\text{-ClC}_6\text{H}_4\text{CH}=\text{C}(\text{CO}_2\text{H})\text{CONHC}_6\text{H}_4\text{Cl}$ -2 + $2\text{-ClC}_6\text{H}_4\text{CH}=\text{CHCONHC}_6\text{H}_4\text{Cl}$ -2 (—)	742
	Piperidinium acetate/100°	$2\text{-ClC}_6\text{H}_4\text{CH}=\text{C}(\text{CO}_2\text{H})\text{CONHC}_6\text{H}_4\text{Cl}$ -3 + $2\text{-ClC}_6\text{H}_4\text{CH}=\text{CHCONHC}_6\text{H}_4\text{Cl}$ -3 (—)	742
	Piperidinium acetate/100°	$2\text{-ClC}_6\text{H}_4\text{CH}=\text{C}(\text{CO}_2\text{H})\text{CONHC}_6\text{H}_4\text{Cl}$ -4 + $2\text{-ClC}_6\text{H}_4\text{CH}=\text{CHCONHC}_6\text{H}_4\text{Cl}$ -4 (—)	742
	Pyridine/Heat	$2\text{-ClC}_6\text{H}_4\text{CH}=\text{CHCONHC}_6\text{H}_4\text{I}$ -4 (—)	747
$2\text{-Nitrobenzaldehyde}$	Pyridine/100°	$4\text{-ClC}_6\text{H}_4\text{CH}=\text{CHCONHC}_6\text{H}_5$ (70)	101
	None/100°	$4\text{-ClC}_6\text{H}_4\text{CH}=\text{C}(\text{CO}_2\text{H})\text{CONHC}_6\text{H}_5$ (6)	101
	Piperidinium acetate/100°	$4\text{-ClC}_6\text{H}_4\text{CH}=\text{C}(\text{CO}_2\text{H})\text{CONHC}_6\text{H}_5$ (66)	101
	Piperidinium acetate/100°	$4\text{-ClC}_6\text{H}_4\text{CH}=\text{C}(\text{CO}_2\text{H})\text{CONHC}_6\text{H}_4\text{Cl}$ -2 + $4\text{-ClC}_6\text{H}_4\text{CH}=\text{CHCONHC}_6\text{H}_4\text{Cl}$ -2 (—)	742
$3\text{-Nitrobenzaldehyde}$	Piperidinium acetate/100°	$4\text{-ClC}_6\text{H}_4\text{CH}=\text{C}(\text{CO}_2\text{H})\text{CONHC}_6\text{H}_4\text{Cl}$ -3 + $4\text{-ClC}_6\text{H}_4\text{CH}=\text{CHCONHC}_6\text{H}_4\text{Cl}$ -3 (—)	742
	Piperidinium acetate/100°	$4\text{-ClC}_6\text{H}_4\text{CH}=\text{C}(\text{CO}_2\text{H})\text{CONHC}_6\text{H}_4\text{Cl}$ -4 + $4\text{-ClC}_6\text{H}_4\text{CH}=\text{CHCONHC}_6\text{H}_4\text{Cl}$ -4 (—)	742
	Piperidinium acetate/100°	$4\text{-ClC}_6\text{H}_4\text{CH}=\text{CHCONHC}_6\text{H}_4\text{Cl}$ -4 (—)	742
	Piperidinium acetate/100°	$4\text{-ClC}_6\text{H}_4\text{CH}=\text{CHCONHC}_6\text{H}_4\text{Cl}$ -4 (—)	742
$2\text{-Nitrobenzaldehyde}$	Piperidine + pyridine or none/100°	$2\text{-O}_2\text{NC}_6\text{H}_4\text{CH}=\text{CHCONHC}_6\text{H}_5$ (mixture of isomers) (45)	102, 743, 744
$3\text{-Nitrobenzaldehyde}$	Piperidine + pyridine/100°	$2\text{-O}_2\text{NC}_6\text{H}_4\text{CH}=\text{C}(\text{CO}_2\text{H})\text{CONHC}_6\text{H}_5$ (—)	102
	Piperidine + pyridine or none/100°	$2\text{-O}_2\text{NC}_6\text{H}_4\text{CH}=\text{C}(\text{CO}_2\text{H})\text{CONHC}_6\text{H}_4\text{CH}_3$ -2 (Good)	743, 744
	Piperidine + pyridine or none/100°	$3\text{-O}_2\text{NC}_6\text{H}_4\text{CH}=\text{CHCONHC}_6\text{H}_5$ (67)	743, 744
$4\text{-Nitrobenzaldehyde}$	Piperidine + pyridine or none/100°	$4\text{-O}_2\text{NC}_6\text{H}_4\text{CH}=\text{CHCONHC}_6\text{H}_5$ (71)	743, 744
Benzaldehyde	Piperidine + pyridine/100°	$\text{C}_6\text{H}_5\text{CH}=\text{CHCONHC}_6\text{H}_5$ (90)	743, 745
	None/100°	$\text{C}_6\text{H}_5\text{CH}=\text{C}(\text{CO}_2\text{H})\text{CONHC}_6\text{H}_5$ (86)	745
	Piperidine + pyridine/steam bath	$\text{C}_6\text{H}_5\text{CH}=\text{CHCONH}_2$ (57)	100
	Piperidine + pyridine/100°	$\text{C}_6\text{H}_5\text{CH}=\text{CHCONHC}_6\text{H}_3(\text{CH}_3)_2$ -2,5 (85)	746
	Pyridine/heat	$\text{C}_6\text{H}_5\text{CH}=\text{CHCONHC}_6\text{H}_4\text{I}$ -4 (—)	747

Note: References 285 to 1153 are on pp. 582–599.

TABLE IV—Continued
CONDENSATIONS WITH MALONAMIC ACIDS OR MALONAMIDES

354

C. Aromatic Aldehydes—Continued			
Aldehyde or Ketone	Catalyst/Temperature	Product(s) and Yield(s) (%)	Refs.
Salicylaldehyde	Piperidine + pyridine/100°	 CONHC ₆ H ₅ (38)	102, 743, 745
	Piperidine + pyridine/100°	 CONHC ₆ H ₄ CH ₃ -2 (—)	102
	Piperidine + pyridine/100°	 CONHC ₆ H ₄ CH ₃ -3 (—)	102
	Piperidine + pyridine/100°	 CONHC ₆ H ₃ (CH ₃) ₂ -2,5 (25)	746
	Pyridine/heat	 CONHC ₆ H ₄ I-4 (—)	747
3-Hydroxybenzaldehyde	Piperidine + pyridine/100°	3-HOC ₆ H ₄ CH=CHCONHC ₆ H ₅ (80)	743
	None/water bath	3-HOC ₆ H ₄ CH=C(CO ₂ H)CONHC ₆ H ₅ (52)	745
4-Hydroxybenzaldehyde	Piperidine + pyridine/water bath	4-HOC ₆ H ₄ CH=CHCONHC ₆ H ₅ (76–80)	693, 743
	None/water bath	4-HOC ₆ H ₄ CH=C(CO ₂ H)CONHC ₆ H ₅ (18)	745
3,4-Dihydroxybenzaldehyde (protocatechuic aldehyde)	Piperidine + pyridine/85°	3,4-(HO) ₂ C ₆ H ₃ CH=CHCONHC ₆ H ₅ (Quant.)	975
6-Bromo-3,4-methylenedioxybenzaldehyde (6-bromopiperonal)	Piperidinium acetate/85°	6-Br-3,4-(CH ₂ O) ₂ C ₆ H ₂ CH=C(CO ₂ H)CONHC ₆ H ₄ CH ₃ -2 (75)	748
	Piperidine + pyridine/100°	6-Br-3,4-(CH ₂ O) ₂ C ₆ H ₂ CH=CHCONHC ₆ H ₄ CH ₃ -2 (43)	748
6-Nitro-3,4-methylenedioxybenzaldehyde (6-nitropiperonal)	Piperidine/water bath	6-Br-3,4-(CH ₂ O) ₂ C ₆ H ₂ CH=CHCONHC ₆ H ₅ (91)	749
	None/100°	6-NO ₂ -3,4-(CH ₂ O) ₂ C ₆ H ₂ CH=C(CO ₂ H)CONHC ₆ H ₄ CH ₃ -2 (39)	748
	Pyridinium acetate/100°	6-NO ₂ -3,4-(CH ₂ O) ₂ C ₆ H ₂ CH=CHCONHC ₆ H ₄ CH ₃ -2 (74)	748
	Pyridine/water bath	6-O ₂ N-3,4-(CH ₂ O) ₂ C ₆ H ₂ CH=CHCONHC ₆ H ₅ (77)	749
3,4-Methylenedioxybenzaldehyde (piperonal)	Piperidine + pyridine/40–60°	3,4-(CH ₂ O) ₂ C ₆ H ₂ CH=CHCONHC ₆ H ₅ (56)	102, 743
	Piperidine + pyridine/45–50°	3,4-(CH ₂ O) ₂ C ₆ H ₂ CH=C(CO ₂ H)CONHC ₆ H ₅ (—)	—
	None/100°	3,4-(CH ₂ O) ₂ C ₆ H ₂ CH=CHCONHC ₆ H ₄ CH ₃ -2 (—)	102
	Piperidinium acetate/100°	3,4-(CH ₂ O) ₂ C ₆ H ₂ CH=C(CO ₂ H)CONHC ₆ H ₄ CH ₃ -2 (—)	750
	None/100°	3,4-(CH ₂ O) ₂ C ₆ H ₂ CH=CHCONHC ₆ H ₄ Cl-2 (85)	750
	Piperidinium acetate/100°	3,4-(CH ₂ O) ₂ C ₆ H ₂ CH=C(CO ₂ H)CONHC ₆ H ₄ Cl-3 (—)	750
	None/100°	3,4-(CH ₂ O) ₂ C ₆ H ₂ CH=CHCONHC ₆ H ₄ Cl-3 (85)	750
	Piperidinium acetate/100°	3,4-(CH ₂ O) ₂ C ₆ H ₂ CH=C(CO ₂ H)CONHC ₆ H ₄ Cl-4 (—)	750
5-Bromo-4-hydroxy-3-methoxybenzaldehyde	Piperidine + pyridine/water bath	3,4-(CH ₂ O) ₂ C ₆ H ₂ CH=CHCONHC ₆ H ₄ Cl-4 (92)	750
	Piperidinium acetate/100°	5-Br-4-HO-3-CH ₃ OC ₆ H ₂ CH=CHCONHC ₆ H ₅ (Low)	749
		5-Br-4-HO-3-CH ₃ OC ₆ H ₂ CH=CHCONHC ₆ H ₄ CH ₃ -2 (Low)	748
4-CH ₃ C ₆ H ₄ CHO	Piperidine + pyridine/water bath	4-CH ₃ C ₆ H ₄ CH=CHCONHC ₆ H ₅ (71)	743
2-CH ₃ OC ₆ H ₄ CHO	Piperidine/110–120°	2-CH ₃ OC ₆ H ₄ CH=CHCONHC ₆ H ₅ (85)	751
3-CH ₃ OC ₆ H ₄ CHO	Pyridine/water bath	3-CH ₃ OC ₆ H ₄ CH=CHCONHC ₆ H ₅ (92)	751
4-CH ₃ OC ₆ H ₄ CHO (anisaldehyde)	Piperidine + pyridine/40–50°	4-CH ₃ OC ₆ H ₄ CH=CHCONHC ₆ H ₅ (—)	102
		4-CH ₃ OC ₆ H ₄ CH=C(CO ₂ H)CONHC ₆ H ₅ (—)	—
	Piperidine/water bath	4-CH ₃ OC ₆ H ₄ CH=CHCONHC ₆ H ₅ (92)	751
3-Methoxy-4-hydroxybenzaldehyde (vanillin)	None/100°	3-CH ₃ O-4-HOC ₆ H ₃ CH=C(CO ₂ H)CONHC ₆ H ₄ Cl-2 (—)	750
	Piperidinium acetate/100°	3-CH ₃ O-4-HOC ₆ H ₃ CH=CHCONHC ₆ H ₄ Cl-2 (88)	750
	None/100°	3-CH ₃ O-4-HOC ₆ H ₃ CH=C(CO ₂ H)CONHC ₆ H ₄ Cl-3 (—)	750
	Piperidinium acetate/100°	3-CH ₃ O-4-HOC ₆ H ₃ CH=CHCONHC ₆ H ₄ Cl-3 (—)	750
	None/100°	3-CH ₃ O-4-HOC ₆ H ₃ CH=C(CO ₂ H)CONHC ₆ H ₄ Cl-4 (—)	750
	Piperidinium acetate/100°	3-CH ₃ O-4-HOC ₆ H ₃ CH=CHCONHC ₆ H ₄ Cl-4 (88)	750
3,4-Dimethoxy-5-bromobenzaldehyde	None/water bath	3,4-(CH ₃ O) ₂ -5-BrC ₆ H ₂ CH=C(CO ₂ H)CONHC ₆ H ₅ (49)	749

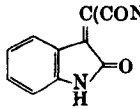
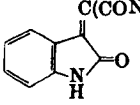
Note: References 285 to 1153 are on pp. 582–599.

ORGANIC REACTIONS

THE KNOEVENAGEL CONDENSATION

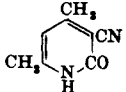
355

TABLE IV—Continued
CONDENSATIONS WITH MALONAMIC ACIDS OR MALONAMIDES

C. Aromatic Aldehydes—Continued			
Aldehyde or Ketone	Catalyst/Temperature	Product(s) and Yield(s) (%)	Refs.
3,4-Dimethoxy-5-bromobenzaldehyde (<i>contd.</i>)	Piperidinium acetate/100°	3,4-(CH ₃ O) ₂ -5-BrC ₆ H ₃ CH=CH-CONHC ₂ H ₅ CH ₃ -2 (Low)	748
3,4-Dimethoxybenzaldehyde (veratraldehyde)	Piperidine + pyridine/40–50°	3,4-(CH ₃ O) ₂ C ₆ H ₃ CH=CHCONHC ₂ H ₅ (—)	102
	Piperidine + pyridine/40–50°	3,4-(CH ₃ O) ₂ C ₆ H ₃ CH=C(CO ₂ H)CONHC ₂ H ₅ (—)	102
		3,4-(CH ₃ O) ₂ C ₆ H ₃ CH=CHCONHC ₂ H ₅ CH ₃ -2 (—)	102
4-(CH ₃) ₂ NC ₆ H ₄ CHO	Piperidine + pyridine/steam bath	3,4-(CH ₃ O) ₂ C ₆ H ₃ CH=C(CO ₂ H)CONHC ₂ H ₅ CH ₃ -2 (—)	100
1-Naphthaldehyde	Piperidine + pyridine/steam bath	4-(CH ₃) ₂ NC ₆ H ₄ CH=CHCONH ₂ (—)	100
		1-C ₁₀ H ₇ CH=CHCONH ₂ (—)	100
D. Heterocyclic Aldehydes and Ketones			
Furfural	Piperidine + pyridine/steam bath	2-C ₄ H ₃ OCH=CHCONH ₂ (—)	100
Isatin	Ethanol NH ₃ /70°	 (76)	98
	Ethanol NH ₃ /70°	 (70)	98

Note: References 285 to 1151 are on pp. 582–599.

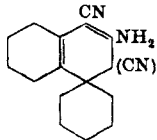
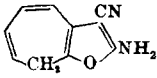
TABLE V
CONDENSATIONS WITH MALONONITRILE


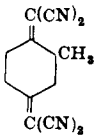

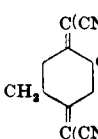

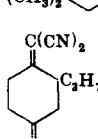
A. Acyclic Aldehydes or Ketones				
Aldehyde or Ketone	Catalyst	Temperature	Product(s) and Yield(s) (%)	Refs.
Acetaldehyde	Piperidine/alcohol	—	$\text{CH}_3\text{CH}=\text{C}(\text{CN})_2$ (—)	752
	$(\text{C}_2\text{H}_5)_3\text{NH}$	0°	$\text{CH}_3\text{CH}[\text{CH}(\text{CN})_2]_2$ (—)	753
Acetone	Piperidine/alcohol	—	$\text{C}_{15}\text{H}_{14}\text{N}_2$ (—)	752
	Piperidine + $\text{CH}_3\text{CO}_2\text{H}$	Steam bath	$(\text{CH}_3)_2\text{C}=\text{C}(\text{CN})_2$ (35)	754
	β -Alanine	Boiling C_6H_6	$(\text{CH}_3)_2\text{C}=\text{C}(\text{CN})_2$ (92)	106
	$\text{CH}_3\text{CO}_2\text{NH}_4$	Boiling CHCl_3	$(\text{CH}_3)_2\text{C}=\text{C}(\text{CN})_2$ (—)	755
$\text{CH}_3\text{COC}_2\text{H}_5$	"	"	$\text{C}_2\text{H}_5\text{C}(\text{CH}_3)=\text{C}(\text{CN})_2$ (—)	755
Acetylacetone	$(\text{C}_2\text{H}_5)_3\text{NH}$	0°	 (77)	99
Diethyl ketone	$\text{CH}_3\text{CO}_2\text{NH}_4$	Boiling C_2H_5 or CHCl_3	$(\text{C}_2\text{H}_5)_2\text{C}=\text{C}(\text{CN})_2$ 90)	104, 754, 755
$\text{CH}_3\text{COC}_2\text{H}_5$ -n	"	Boiling C_2H_5	$n\text{-C}_2\text{H}_5\text{C}(\text{CH}_3)=\text{C}(\text{CN})_2$ (76)	754
$\text{CH}_3\text{COC}_2\text{H}_5$ -i	"	"	$i\text{-C}_2\text{H}_5\text{C}(\text{CH}_3)=\text{C}(\text{CN})_2$ (—)	756
$\text{CH}_3\text{COC}_2\text{H}_5$ -t	β -Alanine	"	$t\text{-C}_2\text{H}_5\text{C}(\text{CH}_3)=\text{C}(\text{CN})_2$ (48)	106
	$\text{CH}_3\text{CO}_2\text{NH}_4$	"	$t\text{-C}_2\text{H}_5\text{C}(\text{CH}_3)=\text{C}(\text{CN})_2$ (—)	756
Ethyl levulinate	"	"	$\text{CH}_3\text{C}=\text{C}(\text{CN})_2$ $\text{CH}_2\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5$ (15)	135
B. Alicyclic Aldehydes or Ketones				
$\triangle\text{COCH}_3$	"	"	$\triangle\text{C}(\text{CH}_3)=\text{C}(\text{CN})_2$ (93)	158

Note: References 285 to 1153 are on pp. 582-599.

* The yield was 82% based on unrecovered ketone.

TABLE V—Continued
CONDENSATIONS WITH MALONONITRILE

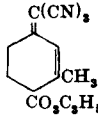
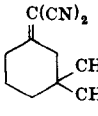
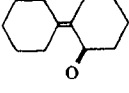

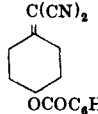
B. Alicyclic Aldehydes or Ketones—Continued				
Aldehyde or Ketone	Catalyst	Temperature	Product(s) and Yield(s) (%)	Refs.
Cyclohexanone	Piperidine	Room	 (30)	103, 105
	"	"	$\text{Cyclohexene}=\text{C}(\text{CN})_2$ (80)	754
	Piperidinium acetate	Boiling C_6H_6	$\text{Cyclohexene}=\text{C}(\text{CN})_2$ (75)	754
	β -Alanine	"	$\text{Cyclohexene}=\text{C}(\text{CN})_2$ (92)	106
	Dowex 3 acetate	"	$\text{Cyclohexene}=\text{C}(\text{CN})_2$ (100)	141
Tropone	Piperidine/ $\text{C}_2\text{H}_5\text{OH}$	Room	 (75)	118
Cyclohexene-4-carboxaldehyde	Piperidine	Boiling C_6H_6	$\text{Cyclohexene}=\text{CH}=\text{C}(\text{CN})_2$ (—)	677

1-Methylcyclohexen-3-one	$\text{CH}_3\text{CO}_2\text{NH}_4$	Boiling CHCl_3	 (87)	757
2-Methylcyclohexane-1,4-dione	β -Alanine	B.p.	 (72)	758
1,5-Dimethylcyclohexen-3-one	$\text{CH}_3\text{CO}_2\text{NH}_4$	Boiling CHCl_3	 (94)	757
2,5-Dimethylcyclohexane-1,4-dione	β -Alanine	Water bath	 (79)	758
1,5,5-Trimethylcyclohexen-3-one	$\text{CH}_3\text{CO}_2\text{NH}_4$	Boiling CHCl_3	 (50)	757
2-n-Propylcyclohexane-1,4-dione	β -Alanine	Room	 (95)	758

Note: References 285 to 1153 are on pp. 582-599.

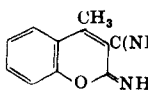
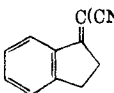
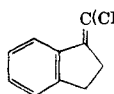
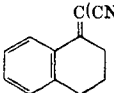
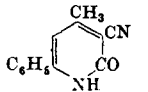
TABLE V—Continued
CONDENSATIONS WITH MALONONITRILE

B. Alicyclic Aldehydes or Ketones—Continued

Aldehyde or Ketone	Catalyst	Temperature	Product(s) and Yield(s) (%)	Refs.
1-Methyl-6-carbethoxy-cyclohexen-3-one	$\text{CH}_3\text{CO}_2\text{NH}_4$	Boiling CHCl_3	 (68)	757
3-Methyl-3-carbomethoxy-methylcyclohexanone	"	Boiling C_2H_5	 (83)	759
	"	"	 (74)	117
4-Benzoyloxy-cyclohexanone	"	"	 (—)	119

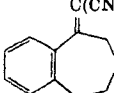
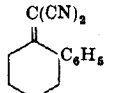
C. Aromatic Aldehydes or Ketones

4-Chloroacetophenone	$\text{CH}_3\text{CO}_2\text{NH}_4$	Boiling C_2H_5	$4\text{-ClC}_6\text{H}_4\text{C}(\text{CH}_3)=\text{C}(\text{CN})_2$ (75)	71
4-Fluoroacetophenone	"	"	$4\text{-FC}_6\text{H}_4\text{C}(\text{CH}_3)=\text{C}(\text{CN})_2$ (79)	71
4-Nitroacetophenone	"	"	$4\text{-O}_2\text{NC}_6\text{H}_4\text{C}(\text{CH}_3)=\text{C}(\text{CN})_2$ (80)	71

Acetophenone	"	"	$C_6H_5C(CH_3)=C(CN)_2$ (70)	71, 115, 756
	$(C_2H_5)_2NH$	Warm ^a	$C_6H_5C(CH_3)=C(CN)_2$ (—)	763
2-Hydroxyacetophenone	Piperidine	Boiling C_2H_5OH	 (13)	112
Indan-1-one	$CH_3CO_2NH_4$	Boiling C_6H_6	 (40)	116
	Pyridine; or piperidine in C_2H_5OH	B.p.	 (—)	763
$CH_3COCH_2C_6H_5$	$CH_3CO_2NH_4$	Boiling $CHCl_3$	$C_6H_5CH_2C(CH_3)=C(CN)_2$ (—)	755
$CH_3CH_2COC_6H_5$	"	Boiling C_6H_6	$C_6H_5C(C_2H_5)=C(CN)_2$ (65)	756
4-Methylacetophenone	"	"	$4-CH_3C_6H_4C(CH_3)=C(CN)_2$ (85)	71
4-Methoxyacetophenone	"	"	$4-CH_3OC_6H_4C(CH_3)=C(CN)_2$ (—)	756
α -Tetralone	"	"	 (79)	71, 756
Benzalacetone	"	"	$C_6H_5CH=CHC(CH_3)=C(CN)_2$ (—)	756
Benzoylacetone	$(C_2H_5)_2NH$	0°	 (10)	99
Butyrophenone	$CH_3CO_2NH_4$	Boiling C_6H_6	$C_6H_5C(C_3H_7-n)=C(CN)_2$ (70)	71
Isobutyrophenone	"	"	$C_6H_5C(C_3H_7-i)=C(CN)_2$ (93)	756

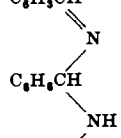
Note: References 285 to 1153 are on pp. 582-599.

TABLE V—Continued
CONDENSATIONS WITH MALONONITRILE

C. Aryl Aldehydes or Ketones—Continued					
Aldehyde or Ketone	Catalyst	Temperature	Product(s) and Yield(s) (%)	Refs.	
3-Ethylacetophenone	$CH_3CO_2NH_4$	Boiling C_6H_6	$3-C_2H_5C_6H_4C(CH_3)=C(CN)_2$ (61)	71	
4-Ethylacetophenone	"	"	$4-C_2H_5C_6H_4C(CH_3)=C(CN)_2$ (60)	71	
2,5-Dimethylacetophenone	"	"	$2,5-(CH_3)_2C_6H_3C(CH_3)=C(CN)_2$ (60)	71	
4-Ethoxyacetophenone	"	"	$4-C_2H_5OC_6H_4C(CH_3)=C(CN)_2$ (78)	71	
2,3-Benzcycloheptanone	"	"	 (46)	116	
4-Dimethylaminocinnamaldehyde	Piperidinium acetate	Boiling C_2H_5OH	$4-(CH_3)_2NC_6H_4CH=CHCH=C(CN)_2$ (88)	760	
$C_6H_5COC_6H_5$	$CH_3CO_2NH_4$	Boiling C_6H_6	$C_6H_5C(C_6H_5)=C(CN)_2$ (88) [†]	756	
3-Phenyl-3-methylbutan-2-one	"	"	$C_6H_5(C(CH_3)_2)CC(CH_3)=C(CN)_2$ (25)	761	
4-Isopropylacetophenone	"	"	$4-i-C_3H_7C_6H_4C(CH_3)=C(CN)_2$ (63)	71	
2-Acetylnaphthalene	"	"	$2-C_{10}H_7C(CH_3)=C(CN)_2$ (—)	756	
2-Phenylcyclohexanone	"	"	 (97)	280	
$4-(CH_3)_2NC_6H_4COCOC_6H_5$	Piperidine	Boiling C_2H_5OH	$4-(CH_3)_2NC_6H_4C(CO_2C_2H_5)=C(CN)_2$ (63)	762	
$C_6H_5COC_6H_{11-n}$	$CH_3CO_2NH_4$	Boiling C_6H_6	$C_6H_5C(C_6H_{11-n})=C(CN)_2$ (61)	71	
4- <i>t</i> -Butylacetophenone	"	"	$4-(CH_3)_3CC_6H_4C(CH_3)=C(CN)_2$ (67)	71	
3,5-Diethylacetophenone	"	"	$3,5-(C_2H_5)_2C_6H_3C(CH_3)=C(CN)_2$ (60)	71	
4-Di-(2'-hydroxyethyl)amino-cinnamaldehyde	Piperidinium acetate	Boiling C_2H_5OH	$4-(HOCH_2CH_2)_2NC_6H_4CH=CHCH=C(CN)_2$ (—)	760	
$C_6H_5COCONHC_6H_5$	$(C_2H_5)_2NH/C_2H_5OH$	Room	$C_6H_5C(CONHC_6H_5)=C(CN)_2$ (90)	163	
Benzil	$C_6H_5N(C_2H_5)_2$	70°	$C_6H_5C(COC_6H_5)=C(CN)_2C(NH_2)=C(CN)_2$ (—)	763	
Benzoin	$(C_2H_5)_2NH$	Warm C_2H_5OH	$C_6H_5CHOHC(C_6H_5)=C(CN)_2$ (—)	763	
4-Acetylbiphenyl	$CH_3CO_2NH_4$	Boiling C_6H_6	$4-C_6H_5C_6H_4C(CH_3)=C(CN)_2$ (74)	71	

Dibenzyl ketone	Ethanol NH ₃	—	(C ₆ H ₅ CH ₂) ₂ C=C(CN) ₂ (—)	764
4-Di-(2'-cyanoethyl)amino-cinnamaldehyde	Piperidinium acetate	Boiling C ₆ H ₅ OH	4-(NCCH ₂ CH ₂) ₂ NC ₆ H ₄ CH=CHCH=C(CN) ₂ (—)	760

D. Aromatic Aldehydes or Ketones

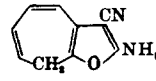
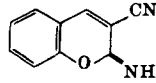
2,4,6-Trichloro-3-hydroxybenzaldehyde	Piperidine/ <i>i</i> -C ₄ H ₉ OH	Room	2,4,6-Cl ₃ -3-HOC ₆ H ₂ CH=C(CN) ₂ (70)	765
2,4-Cl ₂ C ₆ H ₃ CHO	CH ₃ CO ₂ NH ₄ + CH ₃ CONH ₂	Boiling CH ₃ CO ₂ H	2,4-Cl ₂ C ₆ H ₃ CH=C(CN) ₂ (80-90)	766
2,6-Cl ₂ C ₆ H ₃ CHO	Piperidine/C ₂ H ₅ OH	Room	2,6-Cl ₂ C ₆ H ₃ CH=C(CN) ₂ (56)	765
2-Chloro-5-nitrobenzaldehyde	Piperidine/ <i>i</i> -C ₄ H ₉ OH	"	2-Cl-5-O ₂ NC ₆ H ₃ CH=C(CN) ₂ (78)	765
2-BrC ₆ H ₄ CHO	Piperidine/ <i>n</i> -C ₄ H ₉ OH	"	2-BrC ₆ H ₄ CH=C(CN) ₂ (95)	765
	Piperidinium benzoate	Boiling C ₆ H ₆	2-BrC ₆ H ₄ CH=C(CN) ₂ (71)	155
3-BrC ₆ H ₄ CHO	Piperidine/ <i>t</i> -C ₄ H ₉ OH	Room	3-BrC ₆ H ₄ CH=C(CN) ₂ (81)	765
5-Bromosalicylaldehyde	Piperidine/C ₂ H ₅ OH	"	2-HO-5-BrC ₆ H ₃ CH=C(CN) ₂ (80)	110
2-ClC ₆ H ₄ CHO	Piperidine/ <i>t</i> -C ₄ H ₉ OH	"	2-ClC ₆ H ₄ CH=C(CN) ₂ (85)	105
3-ClC ₆ H ₄ CHO	"	"	3-ClC ₆ H ₄ CH=C(CN) ₂ (85)	765
4-ClC ₆ H ₄ CHO	Piperidine/ <i>i</i> -C ₄ H ₉ OH	"	4-ClC ₆ H ₄ CH=C(CN) ₂ (80)	765
3-IC ₆ H ₄ CHO	Piperidine/ <i>t</i> -C ₄ H ₉ OH	"	3-IC ₆ H ₄ CH=C(CN) ₂ (85)	765
2-O ₂ NC ₆ H ₄ CHO	None	Warm	2-O ₂ NC ₆ H ₄ CH=C(CN) ₂ (Quant.)	767
3-O ₂ NC ₆ H ₄ CHO	Piperidine/C ₂ H ₅ OH	Room	3-O ₂ NC ₆ H ₄ CH=C(CN) ₂ (90)	105
4-O ₂ NC ₆ H ₄ CHO	"	"	4-O ₂ NC ₆ H ₄ CH=C(CN) ₂ (41)	765
Benzaldehyde	Piperidine/alcohol	—	C ₆ H ₅ CH=C(CN) ₂ (—)	752
	Piperidine/ <i>t</i> -C ₄ H ₉ OH	Room	C ₆ H ₅ CH=C(CN) ₂ (96)	105
	Piperidine	Boiling C ₆ H ₆	C ₆ H ₅ CH=C(CN) ₂ (74)	69
	+ <i>n</i> -C ₄ H ₉ CO ₂ H	"	C ₆ H ₅ CH=C(CN) ₂ (95)	115
	CH ₃ CO ₂ NH ₄	"	C ₆ H ₅ CH=C(CN) ₂	
				
Benzaldehyde (as benzhydramide)	None	Room	C ₆ H ₅ CHCH(CN) ₂ (—)	19

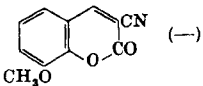
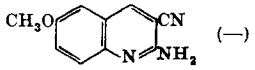
Note: References 285 to 1153 are on pp. 582-599.

† The yield was based on unrecovered ketone.

TABLE V—Continued
CONDENSATIONS WITH MALONONITRILE



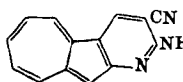
D. Aromatic Aldehydes or Ketones—Continued

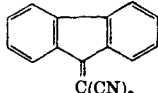

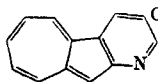
Aldehyde or Ketone	Catalyst	Temperature	Product(s) and Yield(s) (%)	Refs.
Tropone	Piperidine/C ₂ H ₅ OH	Room	 (75)	118
Salicylaldehyde	"	"	2-HOC ₆ H ₄ CH=C(CN) ₂ (78)	110
	"	Ice	 (66)	111
3-Hydroxybenzaldehyde	"	Room	3-HOC ₆ H ₄ CH=C(CN) ₂ (59)	765
	CH ₃ CO ₂ NH ₄ + CH ₃ CONH ₂	Boiling CH ₃ CO ₂ H	3-HOC ₆ H ₄ CH=C(CN) ₂ (80-90)	766
4-Hydroxybenzaldehyde	Piperidine/CH ₃ OH	Room	4-HOC ₆ H ₄ CH=C(CN) ₂ (77)	105
	CH ₃ CO ₂ NH ₄ + CH ₃ CONH ₂	Boiling CH ₃ CO ₂ H	4-HOC ₆ H ₄ CH=C(CN) ₂ (80-90)	766
3,4-Dihydroxybenzaldehyde (protocatechuic aldehyde)	None	Room	3,4-(HO) ₂ C ₆ H ₃ CH=C(CN) ₂ (—)	16
3,4,5-Trihydroxybenzaldehyde	"	Warm	3,4,5-(HO) ₃ C ₆ H ₂ CH=C(CN) ₂ (—)	16
2-Aminobenzaldehyde	CH ₃ CO ₂ NH ₄ + CH ₃ CONH ₂	Boiling CH ₃ CO ₂ H	2-H ₂ NC ₆ H ₄ CH=C(CN) ₂ (80-90)	766
	Piperidinium acetate	Boiling C ₂ H ₅ OH	2-H ₂ NC ₆ H ₄ CH=C(CN) ₂ (30)	762
4-Aminobenzaldehyde	"	"	4-H ₂ NC ₆ H ₄ CH=C(CN) ₂ (78)	762
4-Cyanobenzaldehyde	CH ₃ CO ₂ NH ₄ + CH ₃ CONH ₂	Boiling CH ₃ CO ₂ H	4-NCC ₆ H ₄ CH=C(CN) ₂ (80-90)	766
Terephthalaldehyde	None	Boiling alcohol	4-(NC) ₂ C=CHC ₆ H ₄ CH=C(CN) ₂ (74)	191
3,4-Methylenedioxybenzaldehyde (piperonal)	Piperidine/ <i>n</i> -C ₄ H ₉ OH	Room	3,4-(CH ₂ O) ₂ C ₆ H ₂ CH=C(CN) ₂ (96)	105
6-Hydroxyfulvene-3,4-dicarboxaldehyde	(C ₂ H ₅) ₂ NH/C ₂ H ₅ OH	"	(NC) ₂ C=CH-C ₆ H ₃ (CO ₂ H) ₂ CH=C(CN) ₂ (C ₆ H ₅) ₂ NH ₂ ⁺ (40)	768

2-CH ₃ C ₆ H ₄ CHO	Piperidine/ <i>i</i> -C ₄ H ₉ OH	"	2-CH ₃ C ₆ H ₄ CH=C(CN) ₂ (51)	765
3-CH ₃ C ₆ H ₄ CHO	"	"	3-CH ₃ C ₆ H ₄ CH=C(CN) ₂ (38)	765
			4-CH ₃ C ₆ H ₄ CH=C(CN) ₂	
4-Methylbenzaldehyde (as the benzhydramide)	None	"	4-CH ₃ C ₆ H ₄ CH=C(CN) ₂ (—)	19
			4-CH ₃ C ₆ H ₄ CHCH(CN) ₂	
	CH ₃ CO ₂ NH ₄ + CH ₃ CONH ₂	Boiling CH ₃ CO ₂ H	4-CH ₃ C ₆ H ₄ CH=C(CN) ₂ (80-90)	766
2-Methoxybenzaldehyde	Piperidine/ <i>i</i> -C ₄ H ₉ OH	Room	2-CH ₃ OC ₆ H ₄ CH=C(CN) ₂ (90)	105
4-Methoxybenzaldehyde (anisaldehyde)	Piperidine/CH ₃ OH	"	4-CH ₃ OC ₆ H ₄ CH=C(CN) ₂ (93)	105
	CH ₃ CO ₂ NH ₄ + CH ₃ CONH ₂	Boiling CH ₃ CO ₂ H	4-CH ₃ OC ₆ H ₄ CH=C(CN) ₂ (80-90)	766
2-Hydroxy-3-methoxybenzaldehyde	Piperidine/C ₂ H ₅ OH	Ice	4-CH ₃ OC ₆ H ₄ CH=C(CN) ₂ (86)	111
	—	—	2-HO-3-CH ₃ OC ₆ H ₄ CH=C(CN) ₂ (—)	147
			 (—)	
2-Hydroxy-4-methoxybenzaldehyde	Piperidine/C ₂ H ₅ OH	Room	2-HO-4-CH ₃ OC ₆ H ₄ CH=C(CN) ₂ (90)	110
4-Hydroxy-3-methoxybenzaldehyde (vanillin)	Piperidine/C ₂ H ₅ OH	"	3-CH ₃ O-4-HOC ₆ H ₄ CH=C(CN) ₂ (85)	105
	Piperidine/C ₂ H ₅ OH	Ice	3-CH ₃ O-4-HOC ₆ H ₄ CH=C(CN) ₂ (90)	111
2-Amino-5-methoxybenzaldehyde	Pyridine	Boiling alcohol	 (—)	113
4-Acetoxybenzaldehyde	CH ₃ CO ₂ NH ₄ + CH ₃ CONH ₂	Boiling CH ₃ CO ₂ H	4-CH ₃ CO ₂ C ₆ H ₄ CH=C(CN) ₂ (80-90)	766
4-Methoxybenzene-1,3-dicarboxaldehyde	Piperidine	Boiling C ₂ H ₅ OH	CH ₃ OC ₆ H ₃ (CH=C(CN) ₂) ₂ -2,4 (—)	491

Note: References 285 to 1153 are on pp. 582-599.

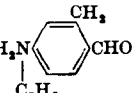
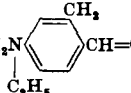
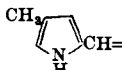
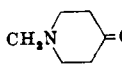
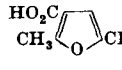
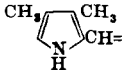
TABLE V—Continued
CONDENSATIONS WITH MALONONITRILE

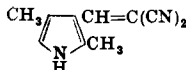
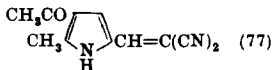
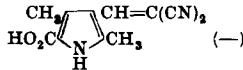
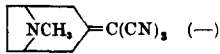
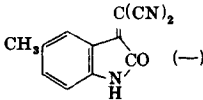
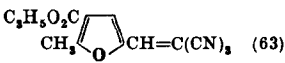
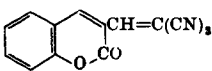
D. Aromatic Aldehydes or Ketones—Continued				
Aldehyde or Ketone	Catalyst	Temperature	Product(s) and Yield(s) (%)	Refs.
4-Acetamidobenzaldehyde	CH ₃ CO ₂ NH ₄ + CH ₃ CONH ₂	Boiling CH ₃ CO ₂ H	4-CH ₃ CONHC ₆ H ₄ CH=C(CN) ₂ (80-90)	766
4-(2'-Chloroethylthio)benzaldehyde	Piperidine/C ₂ H ₅ OH	Room	4-ClCH ₂ CH ₂ SC ₆ H ₄ CH=C(CN) ₂ (87-88)	765
4-(Methoxymethyl)benzaldehyde	"	"	4-CH ₃ OCH ₂ C ₆ H ₄ CH=C(CN) ₂ (72-73)	765
2,4-Dimethoxybenzaldehyde	"	"	2,4-(CH ₃ O) ₂ C ₆ H ₃ CH=C(CN) ₂ (—)	769
2,5-Dimethoxybenzaldehyde	Piperidine/alcohol	"	2,5-(CH ₃ O) ₂ C ₆ H ₃ CH=C(CN) ₂ (95)	770
3,4-Dimethoxybenzaldehyde (veratraldehyde)	"	"	3,4-(CH ₃ O) ₂ C ₆ H ₃ CH=C(CN) ₂ (Quant.)	769
	CH ₃ CO ₂ NH ₄ + CH ₃ CONH ₂	Boiling CH ₃ CO ₂ H	3,4-(CH ₃ O) ₂ C ₆ H ₃ CH=C(CN) ₂ (80-90)	766
2-Chloro-4-dimethylaminobenzaldehyde	Piperidinium acetate	Boiling C ₂ H ₅ OH	2-Cl-4-(CH ₃) ₂ NC ₆ H ₃ CH=C(CN) ₂ (90)	762
4-Dimethylaminobenzaldehyde	CH ₃ CO ₂ NH ₄ + CH ₃ CONH ₂	Boiling CH ₃ CO ₂ H	4-(CH ₃) ₂ NC ₆ H ₄ CH=C(CN) ₂ (80-90)	766
6-Dimethylaminofulvene-3,4-dicarboxaldehyde	(C ₂ H ₅) ₂ NH/C ₂ H ₅ OH	Room	(NC) ₂ C=CH  CH=C(CN) ₂ (75)	768
	Piperidine in ethanol	"	(NC) ₂ C=CH  CHN(CH ₃) ₂ (24)	711
2-Methyl-4-dimethylaminobenzaldehyde	Piperidinium acetate	Boiling C ₂ H ₅ OH	2-CH ₃ -4-(CH ₃) ₂ NC ₆ H ₃ CH=C(CN) ₂ (62)	762
1-Naphthaldehyde	Piperidine/C ₂ H ₅ OH	Room	1-C ₁₀ H ₇ CH=CH(CN) ₂ (70)	765
2-Aminoazulene-1-carboxaldehyde	"	Water bath	 (100)	717, 718
4-Di-(2'-chloroethyl)-aminobenzaldehyde	Piperidine/dioxane	Room	4-(ClCH ₂ CH ₂) ₂ NC ₆ H ₄ CH=C(CN) ₂ (58)	278

2-Chloro-4-diethyl-aminobenzaldehyde	Piperidinium acetate	Boiling C ₂ H ₅ OH	2-Cl-4-(C ₂ H ₅) ₂ NC ₆ H ₄ CH=C(CN) ₂ (89)	762
2,4-bis-(Dimethylamino)benzaldehyde	Piperidine/alcohol	Room	2,4-[(CH ₃) ₂ N] ₂ C ₆ H ₃ CH=C(CN) ₂ (Quant.)	771
4-Di-(2'-cyanoethyl)-aminobenzaldehyde	Piperidinium acetate	Boiling C ₆ H ₆	4-(NCCH ₂ CH ₂) ₂ NC ₆ H ₄ CH=C(CN) ₂ (85)	762
4-Ethyl-(2'-chloroethyl)-aminobenzaldehyde	"	Boiling C ₂ H ₅ OH	4-C ₂ H ₅ (ClCH ₂ CH ₂)NC ₆ H ₄ CH=C(CN) ₂ (79)	762
Fluorenone	NH ₂ or (C ₂ H ₅) ₂ NH	Room	 (86)	772
Benzophenone	NH ₂ /C ₂ H ₅ OH	Warm, then room	(C ₆ H ₅) ₂ C=C(CN) ₂ (13)	772
Benzophenone imine	CH ₃ CO ₂ NH ₄	Boiling C ₆ H ₆	(C ₆ H ₅) ₂ C=C(CN) ₂ (68)	115
	None	Room	(C ₂ H ₅) ₂ C=C(CN) ₂ (—)	164
2-Phenyltropone	Piperidine/(C ₂ H ₅) ₂ O	Room	 (80)	118
2-Acetamidoazulene-1-carboxaldehyde	Piperidine	Boiling C ₂ H ₅ OH	 (77)	717, 718
3,4,5-Triacetoxybenzaldehyde	None	Room	3,4,5-(CH ₃ CO ₂) ₃ C ₆ H ₂ CH=C(CN) ₂ (—)	16
4-Di-(2'-cyanoethyl)amino-benzaldehyde	CH ₃ CO ₂ NH ₄ + CH ₃ CO ₂ H	Boiling C ₆ H ₆	4-(NCCH ₂ CH ₂) ₂ NC ₆ H ₄ CH=C(CN) ₂ (78)	533
4-Di-(2'-cyanoethyl)amino-2-methylbenzaldehyde	"	"	4-(NCCH ₂ CH ₂) ₂ N-2-CH ₃ C ₆ H ₃ CH=C(CN) ₂ (—)	533
3,5-Di-(<i>t</i> -butyl)-4-hydroxybenzaldehyde	Piperidine	"	3,5-(<i>t</i> -C ₄ H ₉) ₂ -4-HOC ₆ H ₃ CH=C(CN) ₂ (—)	724
4-(Methyl- <i>i</i> -octylamino)-benzaldehyde	"	Boiling C ₂ H ₅ OH	4-CH ₃ (<i>i</i> -C ₈ H ₁₇)NC ₆ H ₄ CH=C(CN) ₂ (—)	240, 773

Note: References 285 to 1153 are on pp. 582-599.

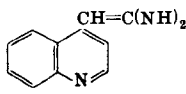
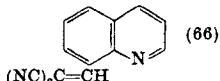
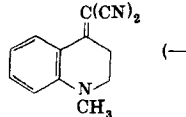
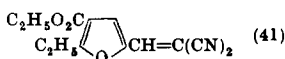
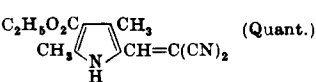
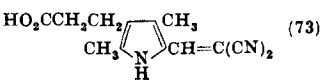
TABLE V—Continued
CONDENSATIONS WITH MALONONITRILE

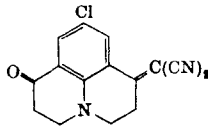
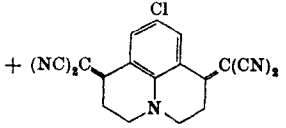
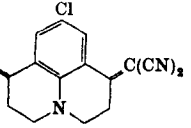
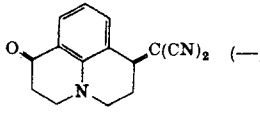
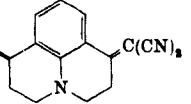
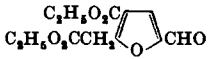
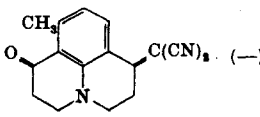
D. Aromatic Aldehydes or Ketones—Continued				
Aldehyde or Ketone	Catalyst	Temperature	Product(s) and Yield(s) (%)	Refs.
	Piperidine/CH ₃ OH	—	 (—)	774
4-Dibenzylaminobenzaldehyde	Piperidinium acetate	Boiling C ₂ H ₅ OH	4-(C ₆ H ₅ CH ₂) ₂ NC ₆ H ₄ CH=C(CN) ₂ (86)	762
E. Heterocyclic Aldehydes or Ketones				
Furfural	C ₆ H ₅ CH ₂ NH ₂ /C ₂ H ₅ OH	Cold	2-C ₆ H ₅ OCH=C(CN) ₂ (97)	381
Thiophene-2-carboxaldehyde	Piperidine/C ₂ H ₅ OH	Room	2-C ₆ H ₅ SCH=C(CN) ₂ (50)	765
	Piperidine	Boiling C ₂ H ₅ OH	2-C ₆ H ₅ SCH=C(CN) ₂ (97)	775
2-Acetylthiophene	CH ₃ CO ₂ NH ₄	Boiling C ₆ H ₆	2-C ₆ H ₅ SC(CH ₃)=C(CN) ₂ (71)	71
4-Methylpyrrole-2-carboxaldehyde	(C ₂ H ₅) ₂ NH/CH ₃ OH	—	 (—)	1142
1-Methyl-4-piperidone	CH ₃ CO ₂ NH ₄	Boiling C ₆ H ₆	 (98)	776
4-Carboxy-5-methylfurfural	(C ₂ H ₅) ₂ NH/alcohol	Room	 (63)	777
3,4-Dimethylpyrrole-2-carboxaldehyde	CH ₃ NH ₂ /C ₂ H ₅ OH	Water bath	 (95)	778

2,4-Dimethylpyrrole-3-carboxaldehyde	$\text{CH}_3\text{NH}_2\text{Cl} + \text{Na}_2\text{CO}_3$	Room	 (73)	779
4-Acetyl-5-methylpyrrole-2-carboxaldehyde	None	—	 (77)	780
2,4-Dimethyl-3-formylpyrrole-5-carboxylic acid	$\text{C}_2\text{H}_5\text{NH}_2/\text{C}_2\text{H}_5\text{OH}$	65°	 (—)	736
Tropanone (tropinone)	$\text{CH}_3\text{CO}_2\text{NH}_4$	Boiling C_2H_5	 (—)	151
5-Methylisatin	—	Boiling $\text{C}_2\text{H}_5\text{OH}$	 (—)	763
4-Carbethoxy-5-methylfurfural	None	Room	 (63)	777
Coumarin-3-carboxaldehyde	„	Warm $\text{C}_2\text{H}_5\text{OH}$	 Quant.	629

Note: References 285 to 1153 are on pp. 582–599.

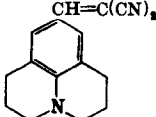
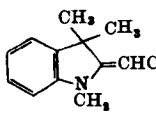
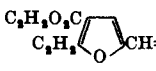
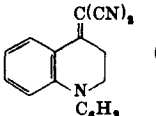
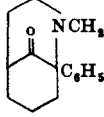
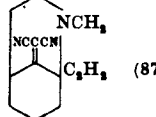
TABLE V—Continued
CONDENSATIONS WITH MALONONITRILE

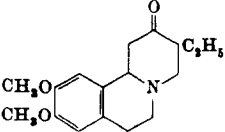
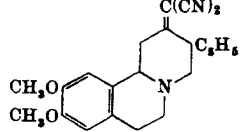
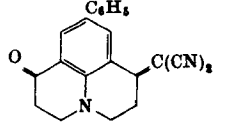
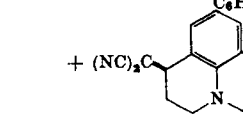
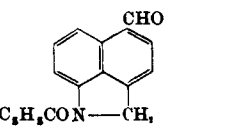
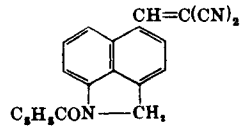
<i>E. Heterocyclic Aldehydes or Ketones—Continued</i>				
Aldehyde or Ketone	Catalyst	Temperature	Product(s) and Yield(s) (%)	Refs.
Quinoline-4-carboxaldehyde hydrate	None or $(\text{C}_2\text{H}_5)_2\text{NH}/\text{C}_2\text{H}_5\text{OH}$	100°	 (65, 98)	42
Quinoline-8-carboxaldehyde	None	Water bath	 (66)	631
N-Methyl-1,2,3,4-tetrahydro-4-quinolone	$\text{CH}_3\text{CO}_2\text{NH}_4$	Boiling C_2H_5	 (—)	109
4-Carbethoxy-5-ethylfurfural	None	Room	 (41)	777
4-Carbethoxy-3,5-dimethylpyrrole-2-carboxaldehyde	$(\text{C}_2\text{H}_5)_2\text{NH}/\text{C}_2\text{H}_5\text{OH}$	„	 (Quant.)	643
3-(2',4'-Dimethyl-5'-formyl-3-pyrrolyl)propionic acid	„	„	 (73)	643

9-Chloro-1,7-diketojulolidine	$\text{CH}_3\text{CO}_2\text{NH}_4$	Boiling C_6H_6	  + $(\text{NC})_2\text{C}$  (—) 109	
1,7-Diketojulolidine	"	"	 + $(\text{NC})_2\text{C}$  (56) 109	
$\text{C}_2\text{H}_5\text{O}_2\text{C}$ $\text{C}_6\text{H}_5\text{O}_2\text{CCH}_2$  CHO	$(\text{C}_2\text{H}_5)_3\text{NH}$	Room	None	777
8-Methyl-1,7-diketojulolidine	$\text{CH}_3\text{CO}_2\text{NH}_4$	Boiling C_6H_6	 (—) 109	

Note: References 285 to 1153 are on pp. 582-599.

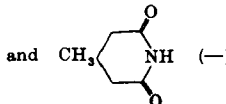





TABLE V—Continued
CONDENSATIONS WITH MALONONITRILE

E. Heterocyclic Aldehydes or Ketones—Continued				
Aldehyde or Ketone	Catalyst	Temperature	Product(s) and Yield(s) (%)	Refs.
Julolidine-9-carboxaldehyde	Piperidinium acetate	Boiling $\text{C}_6\text{H}_5\text{OH}$	 $\text{CH}=\text{C}(\text{CN})_2$ (83)	762
Carbonyl compound not specified	"	"	 $\text{CHCH}=\text{C}(\text{CN})_2$ (40)	762
4-Carboxy-5-phenylfurfural	$(\text{C}_2\text{H}_5)_3\text{NH}/\text{C}_6\text{H}_5\text{OH}$	Room	$\text{C}_2\text{H}_5\text{O}_2\text{C}$ $\text{C}_6\text{H}_5\text{O}_2\text{C}$  $\text{CH}=\text{C}(\text{CN})_2$ (100)	777
8,10-Dimethyl-1,7-diketojulolidine	$\text{CH}_3\text{CO}_2\text{NH}_4$	Boiling C_6H_6	None	109
N-Phenyl-1,2,3,4-tetrahydro-4-quinolone	"	"	 $\text{C}(\text{CN})_2$ (—)	109
	"	"	 NCH_3 C_6H_5 (87)	107

	“	“	 (95)	114
9-Phenyl-1,7-diketolulolidine	“	“		
			 + (NC) ₂ C (—)	109
	Piperidine + pyridine	Water bath	 (—)	662







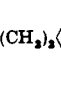





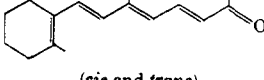

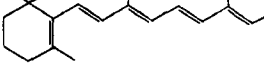

Note: References 285 to 1153 are on pp. 582-599.

TABLE VI
CONDENSATIONS WITH CYANOACETIC ACID

A. Acyclic Aliphatic Aldehydes or Ketones				
Aldehyde or Ketone	Catalyst	Temperature	Product(s) and Yield(s) (%)	Refs.
Acetaldehyde	Piperidine	70°	$\text{CH}_3\text{CH}=\text{C}(\text{CN})\text{CO}_2\text{H}$ (—)	781
	Pyridine	Cold, then heat	$\text{CH}_3\text{CH}=\text{CHCN}$ (—)	782
			$\text{CH}_3\text{CH}(\text{CH}_2\text{CN})_2$ (—)	
			and  (—)	
Propionaldehyde	Piperidine	70°	$\text{C}_2\text{H}_5\text{CH}=\text{C}(\text{CN})\text{CO}_2\text{H}$ (—)	781
	Pyridine	Cold, then heat	$\text{C}_2\text{H}_5\text{CH}=\text{CHCN}$ (25)	783
			and $\text{C}_2\text{H}_5\text{CH}(\text{CH}_2\text{CN})_2$ (—)	
Acetone	Piperidine hydrochloride	Water bath	$(\text{CH}_3)_2\text{C}=\text{C}(\text{CN})\text{CO}_2\text{H}$ (—)	122
	$(\text{C}_2\text{H}_5)_2\text{NH}$	"	$(\text{CH}_3)_2\text{C}(\text{CH}_2\text{CN})\text{CH}(\text{CN})\text{CO}_2\text{H}$ (—)	122
	$\text{CH}_3\text{CO}_2\text{NH}_4$	Boiling C_6H_6	$(\text{CH}_3)_2\text{C}=\text{CHCN}$ (—)	784
	$\text{C}_6\text{H}_5\text{CH}(\text{NH}_2)\text{CO}_2\text{H}$	"	$(\text{CH}_3)_2\text{C}=\text{C}(\text{CN})\text{CO}_2\text{H}$ (94)	106
	β -Alanine	"	$(\text{CH}_3)_2\text{C}=\text{C}(\text{CN})\text{CO}_2\text{H}$ (88)	106
n-Butyraldehyde	Pyridine	Room, then water bath	$n\text{-C}_4\text{H}_9\text{CH}=\text{CHCN}$ (cis and trans) (28)	785
	Piperidine	Steam bath	$n\text{-C}_4\text{H}_9\text{CH}=\text{C}(\text{CN})\text{CO}_2\text{H}$ (75)	786
	Amberlite IR-4B benzoate	Boiling C_6H_6	$n\text{-C}_4\text{H}_9\text{CH}=\text{C}(\text{CN})\text{CO}_2\text{H}$ (100)	128
Isobutyraldehyde	Pyridine	Room, then water bath	$i\text{-C}_4\text{H}_9\text{CH}=\text{CHCN}$ (cis and trans) (80)	130
	Dowex 3	Boiling C_6H_6	$i\text{-C}_4\text{H}_9\text{CH}=\text{C}(\text{CN})\text{CO}_2\text{H}$ (80)	128
$\text{CH}_3\text{COC}_2\text{H}_5$	Amberlite IR-4B acetate	Boiling $\text{CH}_3\text{COC}_2\text{H}_5$	$\text{C}_2\text{H}_5\text{C}(\text{CH}_3)=\text{C}(\text{CN})\text{CO}_2\text{H}$ (6)	128
	$\text{CH}_3\text{CO}_2\text{NH}_4$	Boiling C_6H_6	$\text{C}_2\text{H}_5\text{C}(\text{CH}_3)=\text{CHCN}$ (54)	784
Levulinic Acid	"	"	$\text{NCCH}=\text{C}(\text{CH}_3)\text{CH}_2\text{CH}_2\text{CO}_2\text{H}$ (50)	135
Pentanal	Piperidine	Heat	$n\text{-C}_5\text{H}_{11}\text{CH}=\text{C}(\text{CN})\text{CO}_2\text{H}$ (—)	120
4-Methylbutanal	"	70°	$i\text{-C}_5\text{H}_{11}\text{CH}=\text{C}(\text{CN})\text{CO}_2\text{H}$ (Good)	781
$\text{CH}_3\text{COC}_3\text{H}_7$, n	$\text{CH}_3\text{CO}_2\text{NH}_4$	Boiling C_6H_6	$n\text{-C}_5\text{H}_{11}\text{C}(\text{CH}_3)=\text{CHCN}$ (63)	784
$\text{CH}_3\text{COC}_3\text{H}_7$, i	"	"	$i\text{-C}_5\text{H}_{11}\text{C}(\text{CH}_3)=\text{CHCN}$ (67)	784
Diethyl ketone	"	Boiling C_6H_6 , then 130–140°	$(\text{C}_2\text{H}_5)_2\text{C}=\text{CHCN}$ (72)	126
Mesityl oxide	Piperidine hydrochloride	Water bath	$(\text{CH}_3)_2\text{C}=\text{CHC}(\text{CH}_3)=\text{C}(\text{CN})\text{CO}_2\text{H}$ (—)	122
2-Carboethoxypropionaldehyde	Pyridine	"	$\text{CH}_3\text{C}(\text{CO}_2\text{C}_2\text{H}_5)=\text{CHCH}_2\text{CN}$ (—)	132
Ethyl acetoacetate	Piperidine	100–110°	$\text{CH}_3\text{C}(\text{CH}_3\text{CO}_2\text{C}_2\text{H}_5)=\text{CHCN}$ (18)	136
	$\text{CH}_3\text{CO}_2\text{NH}_4$	Boiling C_6H_6	$\text{NCCH}_2\text{C}(\text{CH}_3)=\text{CHCO}_2\text{C}_2\text{H}_5$ (72)	135
Methyl levulinate	"	"	$\text{NCCH}=\text{C}(\text{CH}_3)\text{CH}_2\text{CH}_2\text{CO}_2\text{CH}_3$ (51)	135
$\text{CH}_3\text{COC}_2\text{H}_5$, n	"	"	$n\text{-C}_4\text{H}_9\text{C}(\text{CH}_3)=\text{CHCN}$ (68)	784
$\text{CH}_3\text{COC}_2\text{H}_5$, i	"	"	$i\text{-C}_4\text{H}_9\text{C}(\text{CH}_3)=\text{CHCN}$ (75)	784
Diethyl mesoxalate	β -Alanine + $\text{CH}_3\text{CO}_2\text{H}$	"	$(\text{C}_2\text{H}_5\text{O}_2\text{C})_2\text{C}=\text{CHCN}$ (75)	787
Ethyl levulinate	Piperidine	110–115°	$\text{NCCH}=\text{C}(\text{CH}_3)\text{CH}_2\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5$ (25)	136
	$\text{CH}_3\text{CO}_2\text{NH}_4$	Boiling C_6H_6	$\text{NCCH}=\text{C}(\text{CH}_3)\text{CH}_2\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5$ (78)	135
Heptanal (oenanthal)	Piperidine	Heat	$n\text{-C}_7\text{H}_{15}\text{CH}=\text{C}(\text{CN})\text{CO}_2\text{H}$ (—)	120
$\text{CH}_3\text{COC}_6\text{H}_{11}$, n	$\text{CH}_3\text{CO}_2\text{NH}_4$	Boiling C_6H_6	$n\text{-C}_7\text{H}_{15}\text{C}(\text{CH}_3)=\text{CHCN}$ (69)	784
$\text{CH}_3\text{COCH}_2\text{C}_6\text{H}_9$, i	"	"	$i\text{-C}_7\text{H}_{15}\text{C}(\text{CH}_3)=\text{CHCN}$ (58)	784
$\text{CH}_3\text{COC}_8\text{H}_{17}$, n	"	"	$n\text{-C}_8\text{H}_{17}\text{C}(\text{CH}_3)=\text{CHCN}$ (81)	784
Citral	Pyridine	100–110°	"Citrylideneacetonitrile" (—)	8
	Piperidine	Water bath	"Citrylideneacyanoacetic" acid (—)	120
Benzyl levulinate	$\text{CH}_3\text{CO}_2\text{NH}_4$	Boiling C_6H_6	$\text{NCCH}=\text{C}(\text{CH}_3)\text{CH}_2\text{CH}_2\text{CO}_2\text{CH}_2\text{C}_6\text{H}_5$ (56)	135
B. Alicyclic Aldehydes or Ketones				
Methyl cyclopropyl ketone	$\text{CH}_3\text{CO}_2\text{NH}_4$	Boiling C_6H_6	 $\text{C}(\text{CH}_3)=\text{CHCN}$ (52)	784
Cyclopentanone	"	"	 CH_2CN (75)	784
Cyclohexanone	Piperidine	Water bath	 $\text{CH}(\text{CN})\text{CO}_2\text{H}$ (Good)	38
	$\text{CH}_3\text{CO}_2\text{NH}_4$	Boiling C_6H_6	 CH_2CN (79)	126, 127, 131, 784
	Amberlite IR-4B benzoate	"	 $=\text{C}(\text{CN})\text{CO}_2\text{H}$ (65)	128

Note: References 285 to 1153 are on pp. 582–599.

TABLE VI—Continued
CONDENSATIONS WITH CYANOACETIC ACID

B. Alicyclic Aldehydes or Ketones—Continued				
Aldehyde or Ketone	Catalyst	Temperature	Product(s) and Yield(s) (%)	Refs.
Cyclohexanone (<i>contd.</i>)	Dowex 3B acetate	Boiling C_6H_6	 (54)	141
Cyclohex-3-enecarboxaldehyde	Piperidine	"	 (—)	677
2-Methylcyclohexanone	$CH_3CO_2NH_4$	"	 * (69)	784
3-Methylcyclohexanone	"	"	 (—)	784
4-Methylcyclohexanone	Piperidine	Water bath	 (Good)	38
	$CH_3CO_2NH_4$	Boiling C_6H_6	 (—)	784
5,5-Dimethylcyclohexane-1,3-dione	Piperidine	110–115°	 (—)	136
Hydroxymethylenecamphor	Pyridine	Water bath	 (—)	132
α -Ionone	$CH_3CO_2NH_4$	Boiling C_6H_6	 (—)	125
β -Ionone	$CH_3CO_2NH_4 + CH_3CO_2H$	"	 (74) (two isomers)	125, 788
	$CH_3CO_2NH_4 + CH_3CONH_2$	Boiling C_6H_6 (under nitrogen)	 (83)	789
			 (99)	
 (<i>cis and trans</i>)	$CH_3CO_2NH_4$	Boiling C_6H_6	 (—)	125
	$CH_3CO_2NH_4 + CH_3CONH_2$	"	 (—)	790
C. Aromatic Aldehydes or Ketones				
Acetophenone	Piperidine hydrochloride	Water bath	$C_6H_5C(CH_3)=C(CN)CO_2H$ (—)	122
	$CH_3CO_2NH_4$	Boiling C_6H_6	$C_6H_5C(CH_3)=CHCN$ (72)	784
Cinnamaldehyde	Amberlite IR-4B benzoate	Room	$C_6H_5CH=CHCH=C(CN)CO_2H$ (25)	128

Note: References 285 to 1153 are on pp. 582–599.

* The location of the double bond was not established.

TABLE VI—Continued
CONDENSATIONS WITH CYANOACETIC ACID

378

ORGANIC REACTIONS

THE KNOEVENAGEL CONDENSATION

379

C. Alkyl Aldehydes or Ketones—Continued				
Aldehyde or Ketone	Catalyst	Temperature	Product(s) and Yield(s) (%)	Refs.
$\text{CH}_3\text{COCH}_2\text{C}_6\text{H}_5$	$\text{CH}_3\text{CO}_2\text{NH}_4$	Boiling C_6H_6	$\text{C}_6\text{H}_5\text{CH}_2\text{C}(\text{CH}_3)=\text{CHCN}$ (75)	784
$\text{C}_6\text{H}_5\text{CH}=\text{CHCOCH}_3$	"	"	$\text{C}_6\text{H}_5\text{CH}=\text{CHC}(\text{CH}_3)=\text{C}(\text{CN})\text{CO}_2\text{H}$ (—)	125
α -Carbethoxyphenylacetaldehyde	Pyridine	Water bath	$\text{C}_6\text{H}_5\text{C}(\text{CO}_2\text{C}_6\text{H}_5)=\text{CHCH}_2\text{CN}$ (47)	132
D. Aromatic Aldehydes or Ketones				
$2,4\text{-Cl}_2\text{C}_6\text{H}_3\text{CHO}$	—	—	$2,4\text{-Cl}_2\text{C}_6\text{H}_3\text{CH}=\text{C}(\text{CN})\text{CO}_2\text{H}$ (75)	796
$2\text{-ClC}_6\text{H}_4\text{CHO}$	Amberlite IR-4B benzoate	Room	$2\text{-ClC}_6\text{H}_4\text{CH}=\text{C}(\text{CN})\text{CO}_2\text{H}$ (55)	128
	Piperidine + pyridine	B.p.	$2\text{-ClC}_6\text{H}_4\text{CH}=\text{CHCN}^\dagger$ (45) [†]	67, 795
	"	Steam bath	$2\text{-ClC}_6\text{H}_4\text{CH}=\text{C}(\text{CN})\text{CO}_2\text{H}$ (14)	
$4\text{-ClC}_6\text{H}_4\text{CHO}$	"	B.p.	$2\text{-ClC}_6\text{H}_4\text{CH}=\text{C}(\text{CN})\text{CO}_2\text{H}$ (90)	795
$2\text{-O}_2\text{NC}_6\text{H}_4\text{CHO}$	$\text{C}_6\text{H}_5\text{NH}_2\text{Cl}$	Water bath	$4\text{-ClC}_6\text{H}_4\text{CH}=\text{CHCN}^\dagger$ (72)	67
$3\text{-O}_2\text{NC}_6\text{H}_4\text{CHO}$	"	"	$2\text{-O}_2\text{NC}_6\text{H}_4\text{CH}=\text{C}(\text{CN})\text{CO}_2\text{H}$ (—)	797
	Amberlite IR-4B benzoate	Room	$3\text{-O}_2\text{NC}_6\text{H}_4\text{CH}=\text{C}(\text{CN})\text{CO}_2\text{H}$ (—)	797
$4\text{-O}_2\text{NC}_6\text{H}_4\text{CHO}$	Piperidinium acetate	Boiling CH_3CN	$3\text{-O}_2\text{NC}_6\text{H}_4\text{CH}=\text{C}(\text{CN})\text{CO}_2\text{H}$ (50)	128
Benzaldehyde	$\text{CH}_3\text{NH}_2\text{Cl}$	Water bath	$4\text{-O}_2\text{NC}_6\text{H}_4\text{CH}=\text{C}(\text{CN})\text{CO}_2\text{H}$ (38)	1145
	$\text{C}_6\text{H}_{11}\text{NH}_2$	Heat	$\text{C}_6\text{H}_5\text{CH}=\text{C}(\text{CN})\text{CO}_2\text{H}$ (—)	791
	Alcoholic NH_3	Room	$\text{C}_6\text{H}_5\text{CH}=\text{C}(\text{CN})\text{CO}_2\text{H}$ (—)	121
	Pyridine	110°	$\text{C}_6\text{H}_5\text{CH}=\text{C}(\text{CN})\text{CO}_2\text{NH}_4$ (96)	19, 792
	"	Room, then water bath	$\text{C}_6\text{H}_5\text{CH}=\text{CHCN}$ (60)	793
	"	20°	$\text{C}_6\text{H}_5\text{CH}=\text{CHCN} \parallel$ (cis and trans) (50)	794
	Amberlite IR-4B benzoate	Boiling C_6H_6	$\text{C}_6\text{H}_5\text{CH}=\text{C}(\text{CN})\text{CO}_2\text{H}$ (90)	793
	Piperidine + pyridine	B.p.	$\text{C}_6\text{H}_5\text{CH}=\text{C}(\text{CN})\text{CO}_2\text{H}$ (94)	128
	Pyridine	B.p.	$\text{C}_6\text{H}_5\text{CH}(\text{CH}_2\text{CN})_2 \parallel$ (48)	133
	Piperidine + pyridine	B.p.	$\text{C}_6\text{H}_5\text{CH}=\text{CHCN}$ (40)	67
$2\text{-HOC}_6\text{H}_4\text{CHO}$ (salicylaldehyde)	Amberlite IR-4B benzoate	Room	$\text{C}_6\text{H}_5\text{CH}=\text{CHCN}^{**}$ (55)	67
$4\text{-HOC}_6\text{H}_4\text{CHO}$	Amberlite IR-4B benzoate	"	$2\text{-HOC}_6\text{H}_4\text{CH}=\text{C}(\text{CN})\text{CO}_2\text{H}$ (20)	128
$3,4\text{-Methylenedioxybenzaldehyde}$ (piperonal)	$\text{C}_6\text{H}_5\text{NH}_2\text{Cl}$	Water bath	$4\text{-HOC}_6\text{H}_4\text{CH}=\text{C}(\text{CN})\text{CO}_2\text{H}$ (75)	128
			$3,4\text{-CH}_2\text{O}_2\text{C}_6\text{H}_3\text{CH}=\text{C}(\text{CN})\text{CO}_2\text{H}$ (—)	797
	Alcoholic NH_3	Room	$3,4\text{-CH}_2\text{O}_2\text{C}_6\text{H}_3\text{CH}=\text{C}(\text{CN})\text{CO}_2\text{NH}_4$ (80)	792
	Amberlite IR-4B benzoate	Boiling ($i\text{-C}_4\text{H}_9$) ₂ O	$3,4\text{-CH}_2\text{O}_2\text{C}_6\text{H}_3\text{CH}=\text{C}(\text{CN})\text{CO}_2\text{H}$ (47)	128
	Piperidine + pyridine	B.p.	$3,4\text{-CH}_2\text{O}_2\text{C}_6\text{H}_3\text{CH}=\text{CHCN}^\dagger$ (68)	67
	"	B.p.	$3,4\text{-CH}_2\text{O}_2\text{C}_6\text{H}_3\text{CH}(\text{CH}_2\text{CN})_2 \parallel$ (84)	133
$4\text{-Methoxybenzaldehyde}$ (anisaldehyde)	$\text{C}_6\text{H}_{11}\text{NH}_2$	Heat	$4\text{-CH}_3\text{OC}_6\text{H}_4\text{CH}=\text{C}(\text{CN})\text{CO}_2\text{H}$ (—)	121
	Alcoholic NH_3	Room	$4\text{-CH}_3\text{OC}_6\text{H}_4\text{CH}=\text{CHCN}$ (57)	792
	Piperidine + pyridine	—	$4\text{-CH}_3\text{OC}_6\text{H}_4\text{CH}=\text{CHCN}$ (16)	798
	Amberlite IR-4B benzoate	Room	$4\text{-CH}_3\text{OC}_6\text{H}_4\text{CH}=\text{C}(\text{CN})\text{CO}_2\text{H}$ (40)	128
	Piperidine + pyridine	B.p.	$4\text{-CH}_3\text{OC}_6\text{H}_4\text{CH}=\text{CHCN}^\dagger$ (41)	67
	"	B.p.	$4\text{-CH}_3\text{OC}_6\text{H}_4\text{CH}(\text{CH}_2\text{CN})_2 \parallel$ (78)	133
$3\text{-Methoxy-4-hydroxybenzaldehyde}$ (vanillin)	Alcoholic NH_3	Room	$3\text{-CH}_3\text{O-4-HOC}_6\text{H}_3\text{CH}=\text{C}(\text{CN})\text{CO}_2\text{NH}_4$ (78)	792
	Amberlite IR-4B benzoate	"	$3\text{-CH}_3\text{O-4-HOC}_6\text{H}_3\text{CH}=\text{C}(\text{CN})\text{CO}_2\text{H}$ (65)	128
	Piperidine + pyridine	B.p.	$3\text{-CH}_3\text{O-4-HOC}_6\text{H}_3\text{CH}=\text{CHCN}^\dagger$ (89)	67
	"	B.p.	$3\text{-CH}_3\text{O-4-HOC}_6\text{H}_3\text{CH}(\text{CH}_2\text{CN})_2 \parallel$ (83)	133
$6\text{-Nitro-3,4-methylenedioxybenzaldehyde}$ (6-nitropiperonal)	$\text{C}_6\text{H}_5\text{NH}_2\text{Cl}$	Water bath	$3,4\text{-CH}_2\text{O}_2\text{-6-O}_2\text{NC}_6\text{H}_3\text{CH}=\text{C}(\text{CN})\text{CO}_2\text{H}$ (—)	797
$3\text{-Nitro-4-methoxybenzaldehyde}$	"	Room	$3\text{-O}_2\text{N-4-CH}_3\text{OC}_6\text{H}_3\text{CH}=\text{C}(\text{CN})\text{CO}_2\text{H}$ (Quant.)	797
$3,4\text{-Dimethoxybenzaldehyde}$ (veratraldehyde)	Piperidine + pyridine	B.p.	$3,4\text{-(CH}_3\text{O)}_2\text{C}_6\text{H}_3\text{CH}=\text{CHCN}^\dagger$ (61)	67
	"	B.p.	$3,4\text{-(CH}_3\text{O)}_2\text{C}_6\text{H}_3\text{CH}(\text{CH}_2\text{CN})_2 \parallel$ (83)	133
$4\text{-(CH}_3)_2\text{NC}_6\text{H}_4\text{CHO}$	Pyridine/ $\text{C}_6\text{H}_5\text{OH}$	90°	$4\text{-(CH}_3)_2\text{NC}_6\text{H}_4\text{CH}=\text{C}(\text{CN})\text{CO}_2\text{H}$ (95)	799
$2,4,6\text{-Trimethylbenzaldehyde}$	Piperidine + pyridine	70°	$2,4,6\text{-(CH}_3)_3\text{C}_6\text{H}_2\text{CH}=\text{C}(\text{CN})\text{CO}_2\text{H}$ (—)	1145
$2,3,4\text{-Trimethoxybenzaldehyde}$	"	B.p.	$2,3,4\text{-(CH}_3\text{O)}_3\text{C}_6\text{H}_2\text{CH}=\text{CHCN}^\dagger$ (60)	67
$3,4,5\text{-Trimethoxybenzaldehyde}$	40% Piperidine in pyridine	160°	$3,4,5\text{-(CH}_3\text{O)}_3\text{C}_6\text{H}_2\text{CH}=\text{CHCN}$ (83)	123, 124
			$3,4,5\text{-(CH}_3\text{O)}_3\text{C}_6\text{H}_2\text{CH}(\text{CH}_2\text{CN})_2$ (—)	
	7% Piperidine in pyridine	160°	$3,4,5\text{-(CH}_3\text{O)}_3\text{C}_6\text{H}_2\text{CH}=\text{CHCN}^\dagger$ (—)	123, 124
$4\text{-Di-(2'-chloroethyl)-aminobenzaldehyde}$	Piperidine/dioxane	Room	$4\text{-(ClCH}_2\text{CH}_2)_2\text{NC}_6\text{H}_4\text{CH}=\text{C}(\text{CN})\text{CO}_2\text{H}$ (95)	278



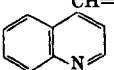
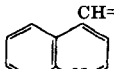
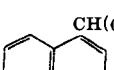
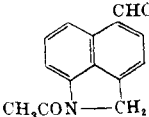
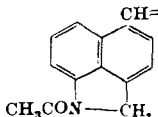
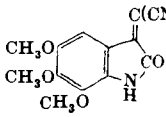
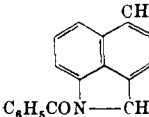
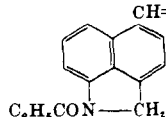
Note: References 285 to 1153 are on pp. 582–599.

- [†] The product was accompanied by some $\text{ArCH}(\text{CH}_2\text{CN})_2$.
- [‡] The yield represents a mixture containing 78% *trans*- and 22% *cis*-cinnamionitrile.
- [§] Benzhydramide was used instead of benzaldehyde.
- ^{||} Some $\text{C}_6\text{H}_5\text{C}(\text{CN})\text{CO}_2\text{H}$ and $\text{C}_6\text{H}_5\text{CH}(\text{CH}_2\text{CN})_2$ were also isolated.
- [¶] Cyanoacetic acid in 100% or greater excess was used.
- ^{**} The product was accompanied by some $\text{ArCH}(\text{CH}_2\text{CN})_2$.
- ^{††} The product was accompanied by some $\text{ArCH}=\text{C}(\text{CN})\text{CO}_2\text{H}$.

TABLE VI—Continued
CONDENSATIONS WITH CYANOACETIC ACID

380

ORGANIC REACTIONS

E. Heterocyclic Aldehydes or Ketones				
Aldehyde or Ketone	Catalyst	Temperature	Product(s) and Yield(s) (%)	Refs.
Furfural	$C_2H_5NH_2$	Heat	$2-C_4H_3OCH=C(CN)CO_2H$ (—)	121
	Alcoholic NH_3	Room	$2-C_4H_3OCH=C(CN)CO_2NH_4$ (58)	792
	Amberlite IR-4B benzoate	"	$2-C_4H_3OCH=C(CN)CO_2H$ (57)	128
	$CH_3CO_2NH_4$	Boiling C_6H_6	$2-C_4H_3OCH=CHCN$ (74–78)	129
Pyridine-2-carboxaldehyde	None	Boiling CH_3OH	None	800
Pyridine-3-carboxaldehyde	"	"	$3-C_5H_4NCH=C(CN)CO_2H$ (82)	800
Pyridine-4-carboxaldehyde	"	Warm	$4-C_5H_4NCH=C(CN)CO_2H$ (68)	800
3-Quinuclidone	$CH_3CO_2NH_4$	Boiling C_6H_6	 CH_2CN (78)	615
			 $CHCN$ (20)	
			$CH=C(CN)CO_2H$	
Quinoline-4-carboxaldehyde hydrate	$(C_2H_5)_2NH/C_2H_5OH$	100°	 (Quant.)	42
	Pyridine + piperidine	100°	 $CH=CHCN$ (80)	42
	"	100°	 $CH(CH_2CN)_2$ ¶ (73)	42
	$CH_3CO_2NH_4 + CH_3CO_2H$	Room	 $CH=C(CN)CO_2H$ (—)	662
5,6,7-Trimethoxyisatin	$(C_2H_5)_3N/dioxane$	Cool	 $C(CN)CO_2H$ (72)	801
	$CH_3CO_2NH_4 + CH_3CO_2H$	Room	 $CH=C(CN)CO_2H$ (—)	662

Note: References 285 to 1153 are on pp. 582–599.

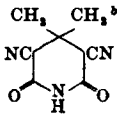
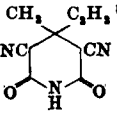
¶ Cyanoacetic acid in 100% or greater excess was used.

THE KNOEVENAGEL CONDENSATION

381

TABLE VII
CONDENSATIONS USING CYANOACETIC ESTERS

When R in $\begin{array}{c} \text{CN} \\ | \\ \text{CH}_2 \\ | \\ \text{CO}_2\text{R} \end{array}$ is not obvious from the product, it is specified in a footnote.

A. Acyclic Aldehydes or Ketones				
Aldehyde or Ketone	Catalyst	Temperature	Product(s) and Yield(s) (%)	Refs.
Acetaldehyde	Piperidinium acetate + Pd/C/H ₂	Room	C ₂ H ₅ CH(CN)CO ₂ C ₂ H ₅ (80-85)	150
	Piperidine/dioxane	Room	CH ₃ CH=C(CN)CO ₂ C ₂ H ₅ (20)	246
	Piperidine/CH ₃ CO ₂ H	Room	CH ₃ CH=C(CN)CO ₂ C ₂ H ₅ (52)	246
CH ₃ COCF ₃	Piperidine + pyridine	0°, then room	CF ₃ C(CH ₃)=C(CN)CO ₂ C ₂ H ₅ (87)	802
Propionaldehyde	Piperidinium acetate + Pd/C and H ₂	Room	n-C ₄ H ₉ CH(CN)CO ₂ C ₂ H ₅ (94)	150
	Pyridine/CH ₃ CO ₂ H	B.p.	C ₂ H ₅ CH(CN)CH(CN)CO ₂ C ₂ H ₅ ^a (53)	803
	Piperidinium acetate	Room	C ₂ H ₅ CH=C(CN)CO ₂ C ₂ H ₅ (63)	246
Acetone	Alcoholic NH ₃		 (—)	804
	(C ₂ H ₅) ₂ NH	Room, then water bath	(CH ₃) ₂ C=C(CN)CO ₂ C ₂ H ₅ (10)	805
	C ₂ H ₅ NH ₂ ·ZnCl ₂	Water bath	(CH ₃) ₂ C[CH(CN)CO ₂ C ₂ H ₅] ₂ (16)	
	CH ₃ NH ₂ ·Cl	" "	(CH ₃) ₂ C=C(CN)CO ₂ C ₂ H ₅ (40)	806
	C ₂ H ₅ NH ₂ ·ZnCl ₂	" "	(CH ₃) ₂ C=C(CN)CO ₂ C ₂ H ₅ (25)	806
	Piperidine	Steam bath	(CH ₃) ₂ C=C(CN)CO ₂ CH ₃ (50) ^c	806
	CH ₃ CONH ₂ + CH ₃ CO ₂ H	110-115°	(CH ₃) ₂ C=C(CN)CO ₂ C ₂ H ₅ (60)	807, 808
			(CH ₃) ₂ C=C(CN)CO ₂ C ₂ H ₅ (30)	46
	CH ₃ CO ₂ NH ₄ + Pd/C and H ₂	Room	(CH ₃) ₂ CHCH(CN)CO ₂ C ₂ H ₅ (—)	150
	CH ₃ CO ₂ NH ₂	Boiling CHCl ₃	(CH ₃) ₂ C=C(CN)CO ₂ C ₂ H ₅ (75)	255, 809
	"	" "	(CH ₃) ₂ C=C(CN)CO ₂ CH ₃ (—)	755
	Pyridine + CH ₃ CO ₂ H	B.p.	(CH ₃) ₂ C(CN)CH(CN)CO ₂ C ₂ H ₅ ^a (70)	803
	Amino acids	Boiling C ₆ H ₆	(CH ₃) ₂ C=C(CN)CO ₂ C ₂ H ₅ (78)	106
	Dowex 3 acetate	" "	(CH ₃) ₂ C=C(CN)CO ₂ C ₂ H ₅ (97)	141
Crotonaldehyde	Piperidine	30°	CH ₃ CH=CHCH=C(CN)CO ₂ C ₂ H ₅ (—) (two forms)	810
n-Butyraldehyde	Piperidinium acetate + Pd/C and H ₂	Room	n-C ₄ H ₉ CH(CN)CO ₂ C ₂ H ₅ (94-96)	150, 277
	Piperidine/dioxane	"	n-C ₄ H ₉ CH=C(CN)CO ₂ C ₂ H ₅ (47)	246
	Piperidinium acetate	"	n-C ₄ H ₉ CH=C(CN)CO ₂ C ₂ H ₅ (74)	246
Isobutyraldehyde	Piperidinium acetate + Pd/C and H ₂	"	i-C ₄ H ₉ CH(CN)CO ₂ C ₂ H ₅ (98)	150
	Pyridine + CH ₃ CO ₂ H	B.p.	i-C ₄ H ₉ CH(CN)CH(CN)CO ₂ C ₂ H ₅ ^a (67)	803
	Piperidine/dioxane	Room	i-C ₄ H ₉ CH=C(CN)CO ₂ C ₂ H ₅ (53)	246
	Piperidine/CH ₃ CO ₂ H	"	i-C ₄ H ₉ CH=C(CN)CO ₂ C ₂ H ₅ (59)	246
C ₂ H ₅ COCH ₃	Aniline chlorozincate	Water bath	C ₂ H ₅ C(CH ₃)=C(CN)CO ₂ C ₂ H ₅ (30)	806
	CH ₃ CONH ₂ /CH ₃ CO ₂ H	110-115°	C ₂ H ₅ C(CH ₃)=C(CN)CO ₂ CH ₃ (40)	46
	CH ₃ CO ₂ NH ₂ or piperidinium acetate	Boiling C ₆ H ₆ or CHCl ₃	C ₂ H ₅ C(CH ₃)=C(CN)CO ₂ C ₂ H ₅ (65-85)	47, 755, 809
	CH ₃ CO ₂ NH ₂ + Pd/C and H ₂	Room	C ₂ H ₅ CH(CH ₃)CH(CN)CO ₂ C ₂ H ₅ (79-81)	150
	Pyridine/CH ₃ CO ₂ H	B.p.	C ₂ H ₅ C(CH ₃) ₂ (CN)CH(CN)CO ₂ C ₂ H ₅ ^a (49)	803
	Amino acids	Boiling C ₆ H ₆	C ₂ H ₅ C(CH ₃)=C(CN)CO ₂ C ₂ H ₅ (80)	106
	NH ₃ , CH ₃ CO ₂ NH ₄	Cold	 (65-70)	811
	Dowex 3 acetate	Boiling C ₂ H ₅	C ₂ H ₅ C(CH ₃)=C(CN)CO ₂ C ₂ H ₅ (97)	141

Note: References 285 to 1153 are on pp. 582-599.

^a The crude product was heated with ethanolic potassium cyanide.

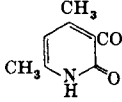
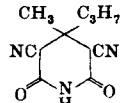
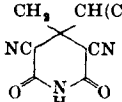
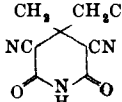
^b Ethyl cyanoacetate was used in this reaction.

^c This yield was based on unrecovered methyl cyanoacetate.

TABLE VII—Continued
CONDENSATIONS USING CYANOACETIC ESTERS

384

ORGANIC REACTIONS

A. Acyclic Aldehydes or Ketones—Continued				
Aldehyde or Ketone	Catalyst	Temperature	Product(s) and Yield(s) (%)	Refs.
Methyl mesoxalate $\text{CH}_3\text{CH}=\text{CHCOCH}_3$	Piperidine $\text{CH}_3\text{CO}_2\text{NH}_4$ $\text{CH}_3\text{CO}_2\text{NH}_4$ + Pd/C and H_2	Steam bath Boiling C_6H_6 Room	$(\text{CH}_3\text{O}_2\text{C})_2\text{C}[\text{CH}(\text{CN})\text{CO}_2\text{CH}_3]_2$ (25) $\text{CH}_3\text{CH}=\text{CHC}(\text{CH}_3)=\text{C}(\text{CN})\text{CO}_2\text{CH}_3$ (57) $n\text{-C}_3\text{H}_7\text{CH}(\text{CH}_3)\text{CH}(\text{CN})\text{CO}_2\text{C}_2\text{H}_5$ (61)	39 812 812
Acetylacetone	$(\text{C}_2\text{H}_5)_2\text{NH}$	Room, then heat	 (42)	145
Valeraldehyde	Piperidine/ $\text{CH}_3\text{CO}_2\text{H}$ Amberlite IR-4B	Room "	$n\text{-C}_4\text{H}_9\text{CH}=\text{C}(\text{CN})\text{CO}_2\text{C}_2\text{H}_5$ (85) $n\text{-C}_4\text{H}_9\text{CH}=\text{C}(\text{CN})\text{CO}_2\text{C}_2\text{H}_5$ (54)	246 181
Isovaleraldehyde	Piperidinium acetate + Pd/C and H_2	"	$i\text{-C}_4\text{H}_9\text{CH}_2\text{CH}(\text{CN})\text{CO}_2\text{C}_2\text{H}_5$ (71)	150
$n\text{-C}_3\text{H}_7\text{COCH}_3$	Piperidine/dioxane $\text{CH}_3\text{CONH}_2/\text{CH}_3\text{CO}_2\text{H}$ $\text{CH}_3\text{CO}_2\text{NH}_4$ or piperidinium acetate $\text{CH}_3\text{CO}_2\text{NH}_4$ $\text{CH}_3\text{CO}_2\text{NH}_4$ + Pd/C and H_2 Dowex 3 acetate	" 110–115° Boiling C_6H_6 " " Room Boiling C_6H_6	$i\text{-C}_4\text{H}_9\text{CH}=\text{C}(\text{CN})\text{CO}_2\text{C}_2\text{H}_5$ (61) $n\text{-C}_3\text{H}_7\text{C}(\text{CH}_3)=\text{C}(\text{CN})\text{CO}_2\text{CH}_3$ (73) $n\text{-C}_3\text{H}_7\text{C}(\text{CH}_3)=\text{C}(\text{CN})\text{CO}_2\text{C}_2\text{H}_5$ (77–85) $n\text{-C}_3\text{H}_7\text{C}(\text{CH}_3)=\text{C}(\text{CN})\text{CO}_2\text{C}_2\text{H}_5$ (80–85) $n\text{-C}_3\text{H}_7\text{CH}(\text{CH}_3)\text{CH}(\text{CN})\text{CO}_2\text{C}_2\text{H}_5$ (63) $n\text{-C}_3\text{H}_7\text{C}(\text{CH}_3)=\text{C}(\text{CN})\text{CO}_2\text{C}_2\text{H}_5$ (90)	246 46 47 47 150 141
$i\text{-C}_3\text{H}_7\text{COCH}_3$	Alcoholic NH_3	40°	 (15)	813
Diethyl ketone	$\text{CH}_3\text{CO}_2\text{NH}_4$ Dowex 3 acetate $\text{CH}_3\text{CONH}_2/\text{CH}_3\text{CO}_2\text{H}$ Piperidine	Boiling C_6H_6 " " 110–115° Steam bath	$i\text{-C}_3\text{H}_7\text{C}(\text{CH}_3)=\text{C}(\text{CN})\text{CO}_2\text{C}_2\text{H}_5$ (64) $i\text{-C}_3\text{H}_7\text{C}(\text{CH}_3)=\text{C}(\text{CN})\text{CO}_2\text{C}_2\text{H}_5$ (65) $(\text{C}_2\text{H}_5)_2\text{C}=\text{C}(\text{CN})\text{CO}_2\text{CH}_3$ (64) $(\text{C}_2\text{H}_5)_2\text{C}=\text{C}(\text{CN})\text{CO}_2\text{C}_2\text{H}_5$ (Low)	756, 814 141 46 807
$(\text{CH}_3)_2\text{C}=\text{CHCOCH}_3$	$\text{CH}_3\text{CO}_2\text{NH}_4$ " " Dowex 3 acetate $\text{CH}_3\text{CO}_2\text{NH}_4$	Boiling C_6H_6 Boiling CHCl_3 Boiling C_6H_6 Boiling CHCl_3	$(\text{C}_2\text{H}_5)_2\text{C}=\text{C}(\text{CN})\text{CO}_2\text{C}_2\text{H}_5$ (75) $(\text{C}_2\text{H}_5)_2\text{C}=\text{C}(\text{CN})\text{CO}_2\text{C}_2\text{H}_5$ (—) $(\text{C}_2\text{H}_5)_2\text{C}=\text{C}(\text{CN})\text{CO}_2\text{C}_2\text{H}_5$ (72) $(\text{CH}_3)_2\text{C}=\text{CHC}(\text{CH}_3)=\text{C}(\text{CN})\text{CO}_2\text{C}_2\text{H}_5$ (—)	47, 276 755, 809 141 755, 809
Ethyl acetoacetate Hexanal	" " Weak base resins	Boiling $\text{CH}_3\text{CO}_2\text{H}$ 100°	$\text{C}_2\text{H}_5\text{O}_2\text{CCH}_2\text{C}(\text{CH}_3)=\text{C}(\text{CN})\text{CO}_2\text{C}_2\text{H}_5$ (19) $n\text{-C}_3\text{H}_7\text{CH}=\text{C}(\text{CN})\text{CO}_2\text{C}_2\text{H}_5$ (33) $n\text{-C}_8\text{H}_{17}\text{CH}[\text{CH}(\text{CN})\text{CO}_2\text{C}_2\text{H}_5]_2$ (12) $(\text{C}_2\text{H}_5)_4\text{CCH}=\text{C}(\text{CN})\text{CO}_2\text{C}_2\text{H}_5$ (83)	135 675 — 181
$(\text{C}_2\text{H}_5)_2\text{CHCHO}$	Amberlite IR-4B or Desacidite Piperidine/dioxane	Cold Room	$(\text{C}_2\text{H}_5)_2\text{CHCH}=\text{C}(\text{CN})\text{CO}_2\text{C}_2\text{H}_5$ (68)	246
$n\text{-C}_4\text{H}_9\text{COCH}_3$	Piperidinium acetate	Boiling C_6H_6	$n\text{-C}_4\text{H}_9\text{C}(\text{CH}_3)=\text{C}(\text{CN})\text{CO}_2\text{C}_2\text{H}_5$ (85)	47
$i\text{-C}_4\text{H}_9\text{COCH}_3$	$\text{CH}_3\text{CONH}_2/\text{CH}_3\text{CO}_2\text{H}$ $\text{CH}_3\text{CO}_2\text{NH}_4$ $\text{CH}_3\text{CO}_2\text{NH}_4$ + Pd/C and H_2 Dowex 3 acetate	110–115° Boiling C_6H_6 Room Boiling C_6H_6 Room Boiling C_6H_6	$i\text{-C}_4\text{H}_9\text{C}(\text{CH}_3)=\text{C}(\text{CN})\text{CO}_2\text{CH}_3$ (76) $i\text{-C}_4\text{H}_9\text{C}(\text{CH}_3)=\text{C}(\text{CN})\text{CO}_2\text{C}_2\text{H}_5$ (75) $i\text{-C}_4\text{H}_9\text{CH}(\text{CH}_3)\text{CH}(\text{CN})\text{CO}_2\text{C}_2\text{H}_5$ (41–63) $i\text{-C}_4\text{H}_9\text{C}(\text{CH}_3)=\text{C}(\text{CN})\text{CO}_2\text{C}_2\text{H}_5$ (85)	46 47 150 141
$sec\text{-C}_4\text{H}_9\text{COCH}_3$	Alcoholic NH_3	40°	 (Very small)	813
$t\text{-C}_4\text{H}_9\text{COCH}_3$ (pinacolone)	$\text{CH}_3\text{CO}_2\text{NH}_4$ Dowex 3 acetate	Boiling C_6H_6 " "	$t\text{-C}_4\text{H}_9\text{C}(\text{CH}_3)=\text{C}(\text{CN})\text{CO}_2\text{C}_2\text{H}_5$ (13) $t\text{-C}_4\text{H}_9\text{C}(\text{CH}_3)=\text{C}(\text{CN})\text{CO}_2\text{C}_2\text{H}_5$ (7)	137, 815 141
Ethyl mesoxalate (as hydrate)	Piperidine	Room	$(\text{C}_2\text{H}_5\text{O}_2\text{C})_2\text{C}=\text{C}(\text{CN})\text{CO}_2\text{C}_2\text{H}_5$ (—)	816
5-Methylhex-5-en-2-one	" "	" "	$(\text{C}_2\text{H}_5\text{O}_2\text{C})_2\text{C}[\text{CH}(\text{CN})\text{CO}_2\text{CH}_3]_2$ (—)	816
	" "	Steam bath	$(\text{C}_2\text{H}_5\text{O}_2\text{C})_2\text{C}=\text{C}(\text{CN})\text{CO}_2\text{CH}_3$ (42)	39
	$\text{CH}_3\text{CO}_2\text{NH}_4$	Boiling C_6H_6	$\text{CH}_2=\text{C}(\text{CH}_3)\text{CH}_2\text{CH}_2\text{C}(\text{CH}_3)=\text{C}(\text{CN})\text{CO}_2\text{C}_4\text{H}_9$ (75)	817
Ethyl levulinate	Alcoholic NH_3	0°	 (—)	833

Note: References 285 to 1153 are on pp. 582–599.

^b Ethyl cyanoacetate was used in this reaction.

^c The catalyst was added in portions.

THE KNOEVENAGEL CONDENSATION

385

TABLE VII—Continued
CONDENSATIONS USING CYANOACETIC ESTERS

386

ORGANIC REACTIONS

A. Acyclic Aldehydes or Ketones—Continued				
Aldehyde or Ketone	Catalyst	Temperature	Product(s) and Yield(s) (%)	Refs.
Ethyl levulinate (<i>contd.</i>)	CH ₃ CONH ₂ Piperazinium diacetate CH ₃ CO ₂ NH ₄ CH ₃ CO ₂ NH ₄ + Pd/C and H ₂	Boiling CH ₃ CO ₂ H Boiling C ₆ H ₅ CH ₃ Boiling C ₆ H ₅ Room	C ₂ H ₅ O ₂ CC(CN)=C(CH ₃)CH ₂ CH ₂ CO ₂ C ₂ H ₅ (60) C ₂ H ₅ O ₂ CC(CN)=C(CH ₃)CH ₂ CH ₂ CO ₂ C ₂ H ₅ (85) C ₂ H ₅ O ₂ CC(CN)=C(CH ₃)CH ₂ CH ₂ CO ₂ C ₂ H ₅ (65) C ₂ H ₅ O ₂ CCH(CN)CH(CH ₃)CH ₂ CH ₂ CO ₂ C ₂ H ₅ (63)	818 819 135 135
Heptanal (oenanthal)	Piperidine Piperidinium acetate + Pd/C and H ₂ Amberlite IR-4B or Deacidite Weak base resins ^a	" " " Cold 100°	n-C ₆ H ₁₃ CH=C(CN)CO ₂ C ₂ H ₅ (32) n-C ₇ H ₁₅ CH(CN)CO ₂ C ₂ H ₅ (71) n-C ₆ H ₁₃ CH=C(CN)CO ₂ C ₂ H ₅ (62)	820 150 181
n-C ₈ H ₁₇ COCH ₃	Piperidine/CH ₃ CO ₂ H CH ₃ CONH ₂ /CH ₃ CO ₂ H CH ₃ CO ₂ NH ₄ CH ₃ CO ₂ NH ₄ + Pd/C and H ₂	Room 110–115° Boiling C ₆ H ₅ Room	n-C ₈ H ₁₇ CH=C(CN)CO ₂ C ₂ H ₅ (25) n-C ₈ H ₁₇ CH[CH(CN)CO ₂ C ₂ H ₅] ₂ (6) n-C ₈ H ₁₇ CH=C(CN)CO ₂ C ₂ H ₅ (85) n-C ₈ H ₁₇ C(CH ₃)=C(CN)CO ₂ C ₂ H ₅ (91) n-C ₈ H ₁₇ C(CH ₃)=C(CN)CO ₂ C ₂ H ₅ (80) n-C ₈ H ₁₇ CH(CH ₃)CH(CN)CO ₂ C ₂ H ₅ (71)	246 46 47 150
(n-C ₈ H ₁₇) ₂ CO	Dowex 3 acetate CH ₃ CONH ₂ /CH ₃ CO ₂ H CH ₃ CO ₂ NH ₄ CH ₃ CO ₂ NH ₄ + Pd/C and H ₂	Boiling C ₆ H ₅ 110–115° Boiling C ₆ H ₅ Room	n-C ₈ H ₁₇ C(CH ₃)=C(CN)CO ₂ C ₂ H ₅ (96) (n-C ₈ H ₁₇) ₂ C=C(CN)CO ₂ C ₂ H ₅ (73) (n-C ₈ H ₁₇) ₂ C=C(CN)CO ₂ C ₂ H ₅ (80) (n-C ₈ H ₁₇) ₂ CHCH(CN)CO ₂ C ₂ H ₅ (39)	46 47 150
Ethyl 2-ketosuccinate	Piperidine	Water bath	C ₂ H ₅ O ₂ CCH ₂ C(CO ₂ C ₂ H ₅)=C(CN)CO ₂ C ₂ H ₅ (—)	821
Ethyl 5-ketohexanoate	Alcoholic NH ₃	0°	$ \begin{array}{c} \text{CH}_3 \quad (\text{CH}_3)_2\text{CO}_2\text{C}_2\text{H}_5^b \\ \diagup \quad \diagdown \\ \text{NC} \quad \text{CN} \\ \diagdown \quad \diagup \\ \text{O} \quad \text{N} \quad \text{O} \\ \quad \quad \\ \quad \quad \text{H} \end{array} $ (—)	65
n-C ₈ H ₁₇ COCH ₃	NH ₃ /C ₂ H ₅ OH	Room	$ \begin{array}{c} \text{CH}_3 \quad \text{C}_6\text{H}_{13}\text{-n}^b \\ \diagup \quad \diagdown \\ \text{NO} \quad \text{CN} \\ \diagdown \quad \diagup \\ \text{O} \quad \text{N} \quad \text{O} \\ \quad \quad \\ \quad \quad \text{H} \end{array} $ (—)	804, 823
2-Ethylhexanal	CH ₃ CONH ₂ /CH ₃ CO ₂ H CH ₃ CO ₂ NH ₄ Piperidine CH ₃ CO ₂ NH ₄ + Pd/C and H ₂ Amberlite IR-4B or Deacidite	110–115° Boiling C ₆ H ₅ Boiling C ₆ H ₅ CH ₃ Room "	n-C ₈ H ₁₇ C(CH ₃)=C(CN)CO ₂ C ₂ H ₅ (90) n-C ₈ H ₁₇ C(CH ₃)=C(CN)CO ₂ C ₂ H ₅ (80) n-C ₈ H ₁₇ C(CH ₃)=C(CN)CO ₂ C ₂ H ₅ (80) n-C ₈ H ₁₇ CH(CH ₃)CH(CN)CO ₂ C ₂ H ₅ (73–81)	46 47 823 150
Ethyl 3-ketoglutarate	Piperazinium diacetate	Boiling C ₆ H ₅	(C ₂ H ₅ O ₂ CCH ₂) ₂ C=C(CN)CO ₂ C ₂ H ₅ (30)	819
Ethyl 6-ketoheptanoate	CH ₃ CONH ₂	—	C ₂ H ₅ O ₂ C(CH ₂) ₄ C(CH ₃)=C(CN)CO ₂ C ₂ H ₅ (—)	824
Ethyl 4-methyl-5-ketohexanoate	"	—	CH ₃ CHCH ₂ CH ₂ CO ₂ C ₂ H ₅ (—)	824
(i-C ₄ H ₉) ₂ CO	CH ₃ CO ₂ NH ₄ Dowex 3 acetate	Boiling C ₆ H ₅ " "	CH ₃ C=C(CN)CO ₂ C ₂ H ₅ (i-C ₄ H ₉) ₂ C=C(CN)CO ₂ C ₂ H ₅ (40) (i-C ₄ H ₉) ₂ C=C(CN)CO ₂ C ₂ H ₅ (6)	47 141
3-(3'-Ketobutyl)-4-methyl-γ-valerolactone	CH ₃ CO ₂ NH ₄ /CH ₃ CO ₂ H	" "	$ \begin{array}{c} \text{CH}_2\text{CH}_2\text{C}(\text{CH}_3)=\text{C}(\text{CN})\text{CO}_2\text{C}_2\text{H}_5 \\ \\ \text{O} \quad \text{O} \end{array} $ (92)	825
Ethyl 5-methyl-6-ketoheptanoate	CH ₃ CO ₂ NH ₄	" "	CH ₃ C(CH ₃)CH ₂ CH ₂ CO ₂ C ₂ H ₅ =C(CN)CO ₂ C ₂ H ₅ (—)	826
Decanal	Piperidine/dioxane	Room	n-C ₈ H ₁₇ CH=C(CN)CO ₂ C ₂ H ₅ (75)	246
n-C ₈ H ₁₇ COCH ₃	Alcoholic NH ₃	"	$ \begin{array}{c} \text{CH}_3 \quad \text{C}_6\text{H}_{17}\text{-n}^b \\ \diagup \quad \diagdown \\ \text{NC} \quad \text{CN} \\ \diagdown \quad \diagup \\ \text{O} \quad \text{N} \quad \text{O} \\ \quad \quad \\ \quad \quad \text{H} \end{array} $ (70)	823

Note: References 285 to 1153 are on pp. 582–599.

^b Ethyl cyanoacetate was used in this reaction.

^a For similar results using various acetals of heptanal see ref. 1146.

THE KNOEVENAGEL CONDENSATION

387

TABLE VII—Continued
CONDENSATIONS USING CYANOACETIC ESTERS

388

ORGANIC REACTIONS

A. Acyclic Aldehydes or Ketones—Continued				
Aldehyde or Ketone	Catalyst	Temperature	Product(s) and Yield(s) (%)	Refs.
2,3,4,5-Diisopropylidene-D-arabinose	$(C_3H_7)_2NH/C_3H_7CH_2$	0°	$\begin{array}{c} CH_3-CH-CH-CH-CH=C(CN)CO_2C_3H_7 \\ \quad \quad \quad \\ O \quad O \quad O \quad O \\ \diagdown \quad \diagup \quad \diagdown \quad \diagup \\ C(CH_3)_2 \quad C(CH_3)_2 \end{array}$	(54) 174
Di-n-amyl ketone $n-C_{10}H_{21}COCH_3$	$CH_3CO_2NH_4$ Piperidine	Boiling C_3H_8 Boiling $C_3H_7CH_3$	$(n-C_8H_{17})_2C=C(CN)CO_2C_3H_7$ (70-87) $n-C_{10}H_{21}C(CH_3)=C(CN)CO_2C_3H_7$ (—)	137, 47 823
	Alcoholic NH_3	Room	$\begin{array}{c} CH_3 \quad C_{10}H_{21}-n^b \\ \quad \\ NC \quad CN \\ \quad \\ O \quad N \quad O \\ \\ H \end{array}$	(—) 823
Dinonyl ketone	$CH_3CO_2NH_4$	Boiling C_3H_8	$(n-C_9H_{19})_2C=C(CN)CO_2C_3H_7$ (79)	137
B. Alicyclic Aldehydes or Ketones				
$\triangle COCH_3$	$CH_3CO_2NH_4$	Boiling C_3H_8	$\triangle C(CH_3)=C(CN)CO_2C_3H_7$ (81) (mixture of isomers)	158
Cyclopentanone	Piperidine	Steam bath	$\text{Cyclopentane ring}-C(CN)CO_2C_3H_7$ (Quant.)	261, 808, 827
	"	—10° to —6°	$\text{Cyclopentane ring}-C(CN)CO_2C_3H_7$ (76)	258
	Alcoholic NH_3	40°	$\begin{array}{c} \text{Cyclopentane ring}^b \\ \quad \\ NC \quad CN \\ \quad \\ O \quad N \quad O \\ \\ H \end{array}$	(50) 813
	$(HOCH_2CH_2)_3N$	Room	$\text{Cyclopentane ring}-C(CN)CO_2C_2H_5$ (40)	58
	CH_3CONH_2/CH_3CO_2H	110–115°	$\text{Cyclopentane ring}-C(CN)CO_2CH_3$ (72)	46
	$CH_3CO_2NH_4$	Boiling $CHCl_3$	$\text{Cyclopentane ring}-C(CN)CO_2C_3H_7$ (—)	809
	"	^a	$\text{Cyclopentane ring}-C(CN)CO_2C_2H_5$ (92)	828
	Dowex 3 acetate	Boiling C_6H_6	$\text{Cyclopentane ring}-C(CN)CO_2C_2H_5$ (100)	141
2-Methylcyclopentanone	Alcoholic NH_3	40°	$\begin{array}{c} \text{Cyclopentane ring}^b \quad CH_3 \\ \quad \\ NC \quad CN \\ \quad \\ O \quad N \quad O \\ \\ H \end{array}$	(Poor) 813

Note: References 285 to 1153 are on pp. 582–599.

^b Ethyl cyanoacetate was used in this reaction.

^a The product was formulated as $\text{Cyclopentane ring}-CH(CN)CO_2C_2H_5$ in ref. 827.

^a The conditions were described as those of ref. 137.

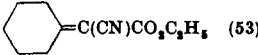
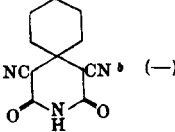
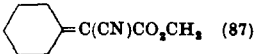
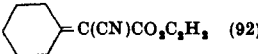
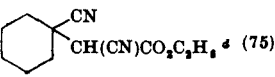
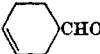
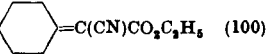
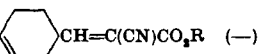
THE KNOEVENAGEL CONDENSATION

389

TABLE VII—Continued
CONDENSATIONS USING CYANOACETIC ESTERS

380

ORGANIC REACTIONS

B. Alicyclic Aldehydes or Ketones—Continued				
Aldehyde or Ketone	Catalyst	Temperature	Product(s) and Yield(s) (%)	Refs.
Cyclohexanone	Piperidine	Steam bath	 (Good, 60, 72) ^b	38, 808, 261
	"	Room	 (53)	820
	Alcoholic NH ₃	30–35°	 (—)	829
	CH ₃ CONH ₂ /CH ₃ CO ₂ H	110–115°	 (87)	46
	CH ₃ CONH ₂	Boiling C ₂ H ₅ , C ₂ H ₅ CH ₃ , or CHCl ₃	 (92)	830, 831
	CH ₃ CO ₂ NH ₄	Boiling C ₂ H ₅ or CHCl ₃	 (83)	47, 809
	CH ₃ CO ₂ NH ₄ + Pd/C and H ₂	Room	 (91–98)	150
	Piperazine	Boiling C ₂ H ₅ CH ₃	 (83)	831
	Pyridine	" "	 (71)	831
	"	Boiling CH ₃ CO ₂ H	 (75)	803
	Dowex 3 acetate	Boiling C ₂ H ₅	 (100)	141
	Piperidine	" "	 (—) A, R = CH ₃	677
	"	" "	A, R = C ₂ H ₅ (96)	677
	"	" "	A, R = C ₂ H ₅ -i (—)	677
	"	" "	A, R = C ₂ H ₅ -n (—)	677
1-Methylcyclohexen-3-one	(C ₂ H ₅) ₂ NH or piperidine	Room, then 120–130°	 (40)	832

Note: References 285 to 1153 are on pp. 582–599.

^b Ethyl cyanoacetate was used in this reaction.

^d The crude product was boiled with ethanolic potassium cyanide.

^a The reaction reported in ref. 261 was done at high pressure.

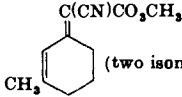
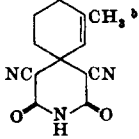
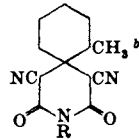
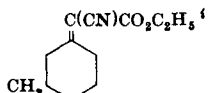
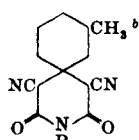
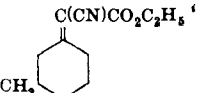
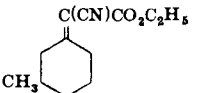
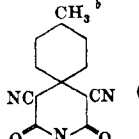
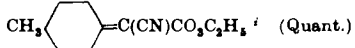

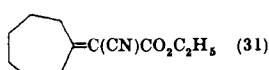
THE KNOEVENAGEL CONDENSATION

391

TABLE VII—Continued
CONDENSATIONS USING CYANOACETIC ESTERS


392

ORGANIC REACTIONS

B. Alicyclic Aldehydes or Ketones—Continued				
Aldehyde or Ketone	Catalyst	Temperature	Product(s) and Yield(s) (%)	Refs.
1-Methylcyclohexen-3-one (contd.)	Piperidine	125°	 (two isomers) (70)	65
	Alcoholic NH ₃	0°	 (60)	65
2-Methylcyclohexanone	NH ₃ or CH ₃ NH ₂ /C ₂ H ₅ OH	30–40°	 (R = H or CH ₃) (Poor)	813, 829
3-Methylcyclohexanone	Piperidine	Room, then heat	 (60)	827
	NH ₃ or CH ₃ NH ₂ /C ₂ H ₅ OH	30–35°	 (R = H or CH ₃) (—)	829
(+)-3-Methylcyclohexanone	Piperidine	Room, then heat	 (—)	834
(±)-3-Methylcyclohexanone	Dowex 3 acetate	Boiling C ₆ H ₆	 (Quant.)	141
4-Methylcyclohexanone	NH ₃ or CH ₃ NH ₂ /C ₂ H ₅ OH	30–35°	 (R = H or CH ₃) (—)	829
	Piperidine	Water bath	 (Quant.)	38
	Dowex 3 acetate	Boiling C ₆ H ₆	 (Quant.)	141
Cycloheptanone	Piperidine	Steam bath	 (31)	808

Note: References 285 to 1153 are on pp. 582–599.

^b Ethyl cyanoacetate was used in this reaction.

^c These compounds were formulated as R-

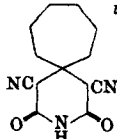
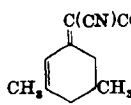
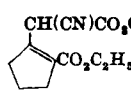
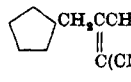
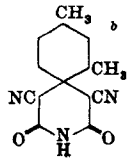
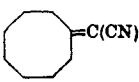
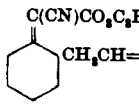
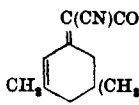
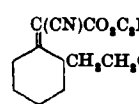
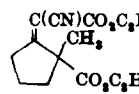
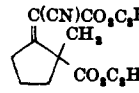
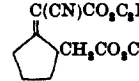
THE KNOEVENAGEL CONDENSATION

393

TABLE VII—Continued
CONDENSATIONS USING CYANOACETIC ESTERS

394

ORGANIC REACTIONS

B. Alicyclic Aldehydes or Ketones—Continued				
Aldehyde or Ketone	Catalyst	Temperature	Product(s) and Yield(s) (%)	Refs.
Cycloheptanone (<i>contd.</i>)	Alcoholic NH_3	Room	 (15)	835
1,5-Dimethylcyclohexen-3-one	$(\text{C}_2\text{H}_5)_3\text{NH}$	Room, then 120–130°	 (40)	832
Ethyl cyclopentanone-2-carboxylate	Piperidine	Room, then steam bath	 (72)	836, 837
Cyclopentylacetone	$\text{CH}_3\text{CO}_2\text{NH}_4$	Boiling C_2H_5	 (87)	822
2,4-Dimethylcyclohexanone	Alcoholic NH_3	40°	 (Poor)	813
Cyclooctanone	$\text{CH}_3\text{CO}_2\text{NH}_4$	Boiling C_2H_5	 (—)	838
2-Allylcyclohexanone	"	" "	 (Mixture) (71)	674
1,5,5-Trimethylcyclohexen-3-one	"	Boiling CHCl_3	 (26)	757
2-(2'-Cyanoethyl)cyclohexanone	"	Boiling C_2H_5	 (68)	839
2-Methyl-2-carbethoxycyclopentanone	Piperidine	Room	 (3)	138
	$\text{CH}_3\text{CO}_2\text{NH}_4$	Boiling C_2H_5	 (90)	840
2-Carbethoxymethylcyclopentanone	Piperidine	Room, then 100°	 (41)	138, 841, 842

Note: References 285 to 1153 are on pp. 582–599.

^b Ethyl cyanoacetate was used in this reaction.

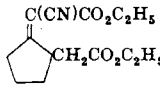
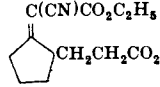
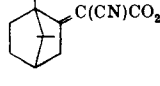
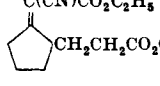
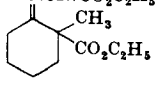
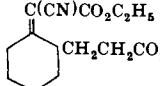
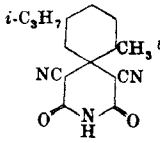
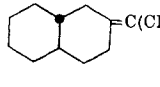
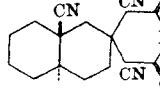



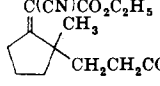
THE KNOEVENAGEL CONDENSATION

395

TABLE VII—Continued
CONDENSATIONS USING CYANOACETIC ESTERS

386

ORGANIC REACTIONS

B. Alicyclic Aldehydes or Ketones—Continued				
Aldehyde or Ketone	Catalyst	Temperature	Product(s) and Yield(s) (%)	Refs.
2-Carboethoxymethylcyclopentanone (contd.)	Piperidine + $\text{C}_6\text{H}_5\text{CH}_2\text{NH}_2$	Room	 (89)	253
2-(β-Carbomethoxyethyl)- cyclopentanone	Piperidine	"	 (17)	138
Camphor	$\text{CH}_3\text{CO}_2\text{NH}_4^*$	Boiling C_6H_6	 (37)	137, 815
2-Carboethoxyethylcyclopentanone	Piperidine	Room	 (33)	138
2-Methyl-2-carboethoxycyclohexanone	$\text{CH}_3\text{CO}_2\text{NH}_4$	Boiling C_6H_6	 (61)	139
2-Carbomethoxyethylcyclohexanone	Piperidine	Room	 (17)	138
2-Methyl-5-isopropylcyclohexanone	Alcoholic NH_3	40°	 (Poor)	813
trans-2-Decalone	Piperidine	Steam bath	 $\text{C}(\text{CN})\text{CO}_2\text{C}_2\text{H}_5$ (—)	808
9-Cyano-trans-2-decalone	$\text{NH}_3/\text{C}_2\text{H}_5\text{OH}$	0°	 (30)	144
	Piperidine	Room, then 100°	 (70)	843
	$\text{NH}_3/\text{C}_2\text{H}_5\text{OH}$	0°	 (40)	843
2-Methyl-2-carboethoxy- ethylcyclopentanone	$\text{CH}_3\text{CO}_2\text{NH}_4$	Boiling C_6H_6	 (35)	844

Note: References 285 to 1153 are on pp. 582–599.

^b Ethyl cyanoacetate was used in this reaction.

* The catalyst was added in portions.

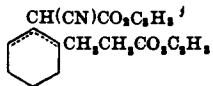
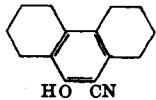
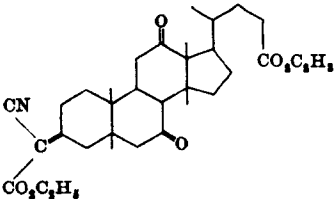
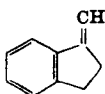
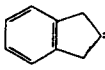
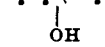
THE KNOEVENAGEL CONDENSATION

387

TABLE VII—Continued
CONDENSATIONS USING CYANOACETIC ESTERS

398

ORGANIC REACTIONS

B. Alicyclic Aldehydes or Ketones—Continued				
Aldehyde or Ketone	Catalyst	Temperature	Product(s) and Yield(s) (%)	Refs.
2-Carboethoxyethylcyclohexanone	Piperidine	Steam bath	 (33)	845
2-Cyclohexylidenecyclohexanone	$\text{CH}_3\text{CO}_2\text{NH}_4$	Boiling C_6H_6	 (34)	117
Ethyl 3,7,12-triketocholanate	$\text{CH}_3\text{CONH}_2/\text{CH}_3\text{CO}_2\text{H}$	105–110°	 (—)	846
C. Condensations with Aromatic Aldehydes or Ketones				
2- $\text{BrC}_6\text{H}_4\text{COCH}_3$	$\text{CH}_3\text{CO}_2\text{NH}_4$	Boiling C_6H_6	2- $\text{BrC}_6\text{H}_4\text{C}(\text{CH}_3)=\text{C}(\text{CN})\text{CO}_2\text{C}_2\text{H}_5$ (85)	847
2- $\text{ClC}_6\text{H}_4\text{COCH}_3$	"	" "	2- $\text{ClC}_6\text{H}_4\text{C}(\text{CH}_3)=\text{C}(\text{CN})\text{CO}_2\text{C}_2\text{H}_5$ (84)	848, 849
4- $\text{ClC}_6\text{H}_4\text{COCH}_3$	"	" "	4- $\text{ClC}_6\text{H}_4\text{C}(\text{CH}_3)=\text{C}(\text{CN})\text{CO}_2\text{C}_2\text{H}_5$ (85)	850
$\text{C}_6\text{H}_5\text{CH}_2\text{CHO}$	Dowex 3 acetate (C_6H_5) ₃ NH	Room	4- $\text{ClC}_6\text{H}_4\text{C}(\text{CH}_3)=\text{C}(\text{CN})\text{CO}_2\text{C}_2\text{H}_5$ (38)	141
			$\text{C}_6\text{H}_5\text{CH}=\text{CHCH}(\text{CN})\text{CO}_2\text{C}_2\text{H}_5$ (25–32)	340
$\text{C}_6\text{H}_5\text{COCH}_3$	Aniline chlorozincate $\text{CH}_3\text{CO}_2\text{NH}_4$	130° Boiling C_6H_6 or CHCl_3	$\text{C}_6\text{H}_5\text{C}(\text{CH}_3)=\text{C}(\text{CN})\text{CO}_2\text{C}_2\text{H}_5$ (30) $\text{C}_6\text{H}_5\text{C}(\text{CH}_3)=\text{C}(\text{CN})\text{CO}_2\text{C}_2\text{H}_5$ (69)	806 47, 137, 756, 809, 851, 852 803
	Pyridine/ $\text{CH}_3\text{CO}_2\text{H}$	B.p.	$\text{C}_6\text{H}_5\text{C}(\text{CN})\text{CH}(\text{CN})\text{CO}_2\text{C}_2\text{H}_5^k$ (17)	
	—	—	CH_3	
2- $\text{HOC}_6\text{H}_4\text{COCH}_3$	$\text{CH}_3\text{CO}_2\text{NH}_4$	Boiling C_6H_6	$\text{C}_6\text{H}_5\text{C}(\text{CH}_3)=\text{C}(\text{CN})\text{CO}_2\text{C}_2\text{H}_5$ (77–79)	853
4- $\text{HOC}_6\text{H}_4\text{COCH}_3$	"	" "	2- $\text{HOC}_6\text{H}_4\text{C}(\text{CH}_3)=\text{C}(\text{CN})\text{CO}_2\text{R}^1$ (—)	854
4- $\text{H}_2\text{NC}_6\text{H}_4\text{COCH}_3$	"	" "	4- $\text{HOC}_6\text{H}_4\text{C}(\text{CH}_3)=\text{C}(\text{CN})\text{CO}_2\text{R}^1$ (—)	854
α -Bromocinnamaldehyde	Piperidine	Room	4- $\text{H}_2\text{NC}_6\text{H}_4\text{C}(\text{CH}_3)=\text{C}(\text{CN})\text{CO}_2\text{C}_2\text{H}_5$ (58–61)	850
Cinnamaldehyde	Piperidine/ $\text{C}_6\text{H}_5\text{OH}$	65°	$\text{C}_6\text{H}_5\text{CH}=\text{CHCH}=\text{C}(\text{CN})\text{CO}_2\text{C}_2\text{H}_5$ (40)	855
	"	30°	$\text{C}_6\text{H}_5\text{CH}=\text{CHCH}=\text{C}(\text{CN})\text{CO}_2\text{C}_2\text{H}_5$ (60)	856
	"	"	('Labile' form)	
	"	"	$\text{C}_6\text{H}_5\text{CH}=\text{CHCH}=\text{C}(\text{CN})\text{CO}_2\text{C}_2\text{H}_5$ (75)	856
	"	"	('Stable' form)	
	Pyridine	Room	$\text{C}_6\text{H}_5\text{CH}=\text{CHCH}=\text{C}(\text{CN})\text{CO}_2\text{C}_2\text{H}_5$ (80)	856
	Piperidine/dioxane	"	$\text{C}_6\text{H}_5\text{CH}=\text{CHCH}=\text{C}(\text{CN})\text{CO}_2\text{C}_2\text{H}_5$ (90)	246
	Piperidine/ $\text{CH}_3\text{CO}_2\text{H}$	"	$\text{C}_6\text{H}_5\text{CH}=\text{CHCH}=\text{C}(\text{CN})\text{CO}_2\text{C}_2\text{H}_5$ (57)	246
Indan-1-one	(C_6H_5) ₃ NH or piperidine	40°	 (55)	143a
Indan-2-one	(C_6H_5) ₃ NH	Below 18°	 (45)	143a
$\text{C}_6\text{H}_5\text{COCO}_2\text{CH}_3$	CH_3NH_2 , NH_3 , or piperidine	0°	$\text{C}_6\text{H}_5\text{C}(\text{CO}_2\text{CH}_3)\text{CH}(\text{CN})\text{CO}_2\text{CH}_3$ (75–80)	37
	$\text{CH}_3\text{NH}_2\text{Cl} + \text{Na}_2\text{CO}_3$	Room	 (70)	37

Note: References 285 to 1153 are on pp. 582–599.

¹ The double bond was said to be probably endocyclic.

² The crude product was treated with boiling ethanolic potassium cyanide.

³ A number of cyanoacetic esters were used.

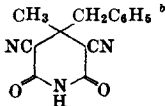
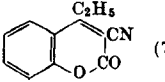
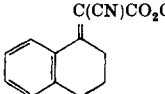
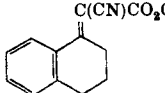
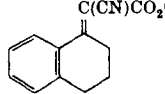
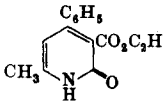
THE KNOEVENAGEL CONDENSATION

399

TABLE VII—Continued
CONDENSATIONS USING CYANOACETIC ESTERS

400

ORGANIC REACTIONS

C. Aromatic Aldehydes or Ketones—Continued				
Aldehyde or Ketone	Catalyst	Temperature	Product(s) and Yield(s) (%)	Refs.
2-Nitrocinnamaldehyde	Piperidine/dioxane	Room	2-O ₂ NC ₆ H ₄ CH=CHCH=C(CN)CO ₂ C ₂ H ₅ (83)	857
2-Methylacetophenone	CH ₃ CO ₂ NH ₄	Boiling C ₆ H ₆	2-CH ₃ C ₆ H ₄ C(CH ₃)=C(CN)CO ₂ C ₂ H ₅ (47)	47
4-Methylacetophenone	"	" "	4-CH ₃ C ₆ H ₄ C(CH ₃)=C(CN)CO ₂ C ₂ H ₅ (70)	756, 850, 858
Propiophenone	Piperidine	Steam bath	C ₆ H ₅ C(C ₂ H ₅)=C(CN)CO ₂ C ₂ H ₅ (—)	152
	CH ₃ CO ₂ NH ₄	Boiling C ₆ H ₆	C ₆ H ₅ C(C ₂ H ₅)=C(CN)CO ₂ C ₂ H ₅ (73)	47, 137, 756, 809, 851, 859
	"	" "	C ₆ H ₅ C(C ₂ H ₅)=C(CN)CO ₂ CH ₃ (64)	859
	Dowex 3 acetate	" "	C ₆ H ₅ C(C ₂ H ₅)=C(CN)CO ₂ C ₂ H ₅ (21)	141
C ₆ H ₅ CH ₂ COCH ₃	Alcoholic NH ₃	40°	 (65)	813
2-CH ₃ OC ₆ H ₄ COCH ₃	Piperidine	Room	C ₆ H ₅ CH ₂ C(CH ₃)=C(CN)CO ₂ C ₂ H ₅ (25)	152
3-CH ₃ OC ₆ H ₄ COCH ₃	Dowex 3 acetate	Boiling C ₆ H ₆	C ₆ H ₅ CH ₂ C(CH ₃)=C(CN)CO ₂ C ₂ H ₅ (12)	141
4-CH ₃ OC ₆ H ₄ COCH ₃	CH ₃ CO ₂ NH ₄	" "	2-CH ₃ OC ₆ H ₄ C(CH ₃)=C(CN)CO ₂ C ₂ H ₅ (79)	851
	"	" "	3-CH ₃ OC ₆ H ₄ C(CH ₃)=C(CN)CO ₂ C ₂ H ₅ (64)	851
	"	" "	4-CH ₃ OC ₆ H ₄ C(CH ₃)=C(CN)CO ₂ C ₂ H ₅ ^m (55)	756, 850, 851, 860
	"	160–180°	4-CH ₃ OC ₆ H ₄ C(CH ₃)=C(CN)CO ₂ C ₂ H ₅ (44)	149
	Dowex 3 acetate	Boiling C ₆ H ₆	4-CH ₃ OC ₆ H ₄ C(CH ₃)=C(CN)CO ₂ C ₂ H ₅ (24)	141
2-Hydroxypropiophenone	CH ₃ CO ₂ NH ₄ ^c	" "	 (75)	148
4-Hydroxypropiophenone	"	" "	4-HOC ₆ H ₄ C(CH ₃)=C(CN)CO ₂ C ₂ H ₅ (45)	137
3,4-Methylenedioxycinnamaldehyde	Piperidine/CH ₃ OH	Room	3,4-CH ₂ O ₂ C ₆ H ₃ CH=CHCH=C(CN)CO ₂ CH ₃ (75)	682
	"	"	3,4-CH ₂ O ₂ C ₆ H ₃ CH=CHCH=C(CN)CO ₂ C ₂ H ₅ (—)	682
C ₆ H ₅ CH=CHCOCH ₃	CH ₃ CO ₂ NH ₄	Boiling C ₆ H ₆	C ₆ H ₅ CH=CHC(CH ₃)=C(CN)CO ₂ C ₂ H ₅ (—)	756
1-Tetralone	"	" "	 (37) ⁿ	861, 862
	C ₆ H ₅ CO ₂ NH ₄	" "	 (48)	861
	Dowex 3 acetate	" "	 (14)	141
Benzoylacetone	(C ₂ H ₅) ₂ NH	Water bath	 (—)	99
4-Methoxycinnamaldehyde	Piperidinium acetate	Boiling C ₂ H ₅ OH	4-CH ₃ OC ₆ H ₄ CH=CHCH=C(CN)CO ₂ C ₂ H ₅ (—)	953
2,4-Dimethylacetophenone	Dowex 3 acetate	Boiling C ₆ H ₆	2,4-(CH ₃) ₂ C ₆ H ₃ C(CH ₃)=C(CN)CO ₂ C ₂ H ₅ (4)	141

Note: References 285 to 1153 are on pp. 582–599.

^b Ethyl cyanoacetate was used in this reaction.

^c The catalyst was added in portions.

^m The yield was 80% based on the acetophenone that reacted.

ⁿ The yield was 70% after allowing for recovered ketone.

THE KNOEVENAGEL CONDENSATION

401

TABLE VII—Continued
CONDENSATIONS USING CYANOACETIC ESTERS

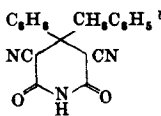
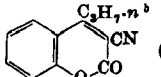
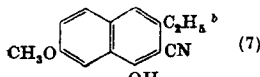
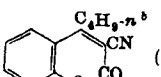
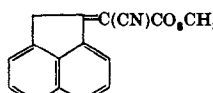
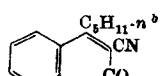
402

ORGANIC REACTIONS

THE KNOEVENAGEL CONDENSATION

403

C. Aromatic Aldehydes or Ketones—Continued

Aldehyde or Ketone	Catalyst	Temperature	Product(s) and Yield(s) (%)	Refs.
Benzylacetone	CH ₃ CO ₂ NH ₄	Boiling C ₆ H ₆	C ₆ H ₅ CH ₂ CH ₂ C(CH ₃)=C(CN)CO ₂ C ₂ H ₅ (64)	47
C ₆ H ₅ CH ₂ COC ₂ H ₅	Alcoholic NH ₃	40°	 (30)	813
C ₆ H ₅ COC ₂ H ₅ -n	CH ₃ CO ₂ NH ₄	Boiling C ₆ H ₆	C ₆ H ₅ C(C ₂ H ₅ -n)=C(CN)CO ₂ C ₂ H ₅ (78)	47, 851
2-Hydroxybutyrophenone	" ^a	" "	 (65)	148
2,5-Dimethoxyacetophenone	"	" "	2,5-(CH ₃ O) ₂ C ₆ H ₃ C(CH ₃)=C(CN)CO ₂ C ₂ H ₅ (80)	863
5-Phenylpentadienal	Piperidine/C ₂ H ₅ OH	Room	C ₆ H ₅ (CH=CH) ₂ CH=C(CN)CO ₂ C ₂ H ₅ (—)	864
4-CH ₃ OC ₆ H ₄ CH=CHCOCH ₃	CH ₃ CO ₂ NH ₄	Boiling C ₆ H ₆	4-CH ₃ OC ₆ H ₄ CH=CHC(CH ₃)=C(CN)CO ₂ C ₂ H ₅ (—)	756
4-Dimethylaminocinnamaldehyde	Piperidinium acetate	Boiling C ₂ H ₅ OH	4-(CH ₃) ₂ NC ₆ H ₄ CH=CHCH=C(CN)CO ₂ C ₂ H ₅ (—)	760
i-C ₃ H ₇ COCH ₂ C ₆ H ₅	Alcoholic NH ₃	40°	None	813
i-C ₄ H ₉ COC ₂ H ₅	Dowex 3 acetate	Boiling C ₆ H ₆	i-C ₄ H ₉ C(C ₂ H ₅)=C(CN)CO ₂ C ₂ H ₅ (6)	141
3-Methoxybutyrophenone	CH ₃ CO ₂ NH ₄	" "	3-CH ₃ OC ₆ H ₄ C(C ₂ H ₅ -n)=C(CN)CO ₂ C ₂ H ₅ (86)	851, 865, 866
4-CH ₃ OC ₆ H ₄ CH ₂ COC ₂ H ₅	"	160°	4-CH ₃ OC ₆ H ₄ CH ₂ C(C ₂ H ₅)=C(CN)CO ₂ C ₂ H ₅ (15)	149
			 (7)	
n-C ₄ H ₉ COC ₂ H ₅ OH-2	CH ₃ CO ₂ NH ₄ ^a	Boiling C ₆ H ₆	 (68)	148
Acenaphthenone		160–180°	 (65)	149
1-Acetylnaphthalene	"	Boiling CH ₃ CO ₂ H	1-C ₁₀ H ₇ C(CH ₃)=C(CN)CO ₂ C ₂ H ₅ (86) ^a	867, 868
2-Acetylnaphthalene	"	" "	1-C ₁₀ H ₇ C(CH ₃)=C(CN)CO ₂ C ₂ H ₅ (72) ^a	868
5-Phenyl-5-cyanopentan-2-one	Piperidine, C ₆ H ₅ CH ₂ NH ₂ and CH ₃ CO ₂ H	" "	2-C ₆ H ₅ C(CH ₃)=C(CN)CO ₂ C ₂ H ₅ (—)	756
			C ₆ H ₅ CH(CN)CH ₂ CH ₂ C(CH ₃)=C(CN)CO ₂ C ₂ H ₅ (62)	869
1-(2'-Methoxyphenyl)pent-4-en-1-one	CH ₃ CO ₂ NH ₄	" "	CH ₃ =CHCH ₂ CH ₂ C(C ₆ H ₄ OCH ₃ -2)=C(CN)CO ₂ R ¹ (—)	854
2,4-Dimethylisobutyrophenone	" ^a	" "	2,4-(CH ₃) ₂ C ₆ H ₃ C(C ₂ H ₅ -i)=C(CN)CO ₂ C ₂ H ₅ (25)	870
1-Phenylhexan-3-one	"	" "	None	815
n-C ₆ H ₁₁ COC ₂ H ₅	"	" "	n-C ₆ H ₁₁ C(C ₂ H ₅)=C(CN)CO ₂ C ₂ H ₅ (87)	137
n-C ₆ H ₁₁ COC ₂ H ₅ OH-2	"	" "	2-HOC ₆ H ₄ C(C ₂ H ₁₁ -n)=C(CN)CO ₂ C ₂ H ₅ (64)	137
			 (70)	148

Note: References 285 to 1153 are on pp. 582–599.

^b Ethyl cyanoacetate was used in this reaction.

^a The catalyst was added in portions.

^c One isomer was isolated in a pure state and postulated as having the structure

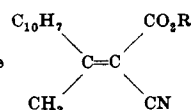
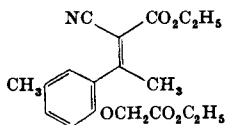
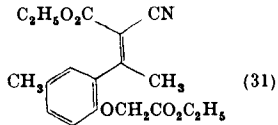
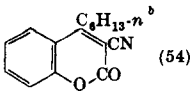
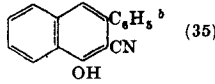
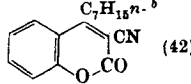
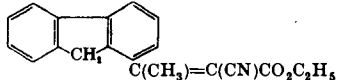


TABLE VII—Continued
CONDENSATIONS USING CYANOACETIC ESTERS

C. Aromatic Aldehydes or Ketones—Continued

Aldehyde or Ketone	Catalyst	Temperature	Product(s) and Yield(s) (%)	Refs.
7-Phenylheptatrienal	Piperidine/C ₂ H ₅ OH	Room	C ₆ H ₅ (CH=CH) ₃ CH=C(CN)CO ₂ C ₂ H ₅ (—)	864
5-(4'-Methoxyphenyl)-5-cyanopentan-2-one	Piperidine, C ₆ H ₅ CH ₂ NH ₂ and CH ₃ CO ₂ H	Boiling C ₆ H ₆	4-CH ₃ OC ₆ H ₄ CH(CN)CH ₂ CH ₂ C(CH ₃)=C(CN)CO ₂ C ₂ H ₅ (52)	871
1-(2'-Hydroxy-4',5'-dimethylphenyl)-pent-2-en-1-one	CH ₃ CO ₂ NH ₄	" "	2-HO-4,5-(CH ₃) ₂ C ₆ H ₃ C(CH=CHC ₂ H ₅)=C(CN)CO ₂ R ¹ (—)	854
1-(4'-Methoxyphenyl)-3-methylpent-2-en-1-one	"	" "	4-CH ₃ OC ₆ H ₄ C(CH=CHC(CH ₃)C ₂ H ₅)=C(CN)CO ₂ R ¹ (—)	854
Ethyl 4-benzoylbutyrate	"Cope's conditions"	" "	C ₂ H ₅ O ₂ C(CH ₂) ₃ C(C ₆ H ₅)=C(CN)CO ₂ C ₂ H ₅ (—)	872
2-Carboethoxymethoxy-5-methylacetophenone	"	Boiling C ₆ H ₆	 (33)	873
			 (31)	
4-Diethylaminocinnamaldehyde	Piperidine	—	4-(C ₂ H ₅) ₂ NC ₆ H ₄ CH=CHCH=C(CN)CO ₂ C ₂ H ₅ (—)	684
C ₆ H ₅ COC ₆ H ₁₃ -n	CH ₃ CO ₂ NH ₄	Boiling C ₆ H ₆	C ₆ H ₅ C(C ₆ H ₁₃ -n)=C(CN)CO ₂ C ₂ H ₅ (75)	47
2-Hydroxyphenyl n-hexyl ketone	CH ₃ CO ₂ NH ₄ ^c	" "	 (54)	148
(CH ₃) ₂ NCH ₂ CH ₂ C(CH ₃)CHO C ₆ H ₅	"	" "	(CH ₃) ₂ NCH ₂ CH ₂ C(CH ₃)CH=CCO ₂ CH ₃ (16) C ₆ H ₅ CN	874
Benzil	(C ₂ H ₅) ₂ NH	C ₂ H ₅ OH, hot	C ₆ H ₅ COC(C ₆ H ₅)=C(CN)CO ₂ C ₂ H ₅ (—)	763
Desoxybenzoin	CH ₃ CO ₂ NH ₄	160°	 (35)	149
1-(2'-Methoxyphenyl)hept-6-en-1-one	"	Boiling C ₆ H ₆	CH ₂ =CH(CH ₂) ₄ C(C ₆ H ₄ OCH ₃ -2)=C(CN)CO ₂ R ¹ (—)	854
Ethyl 2-phenyl-5-ketohexanoate	CH ₃ CONH ₂	—	C ₆ H ₅ CH(CO ₂ C ₂ H ₅)CH ₂ CH ₂ C(CH ₃)=C(CN)CO ₂ C ₂ H ₅ (—)	875
n-C ₇ H ₁₅ COC ₆ H ₅	CH ₃ CO ₂ NH ₄	Boiling C ₆ H ₆	n-C ₇ H ₁₅ C(C ₆ H ₅)=C(CN)CO ₂ C ₂ H ₅ (86)	137
2-HOC ₆ H ₄ COC ₇ H ₁₅ -n	CH ₃ CO ₂ NH ₄ ^c	Boiling C ₆ H ₆	 (42)	148
4-HOC ₆ H ₄ COC ₇ H ₁₅ -n	"	" "	4-HOC ₆ H ₄ C(C ₇ H ₁₅ -n)=C(CN)CO ₂ CH ₃ (—)	854
1-Acetylfluorene	Piperidinium acetate	" "	 (80)	876

Note: References 285 to 1153 are on pp. 582-599.

^b Ethyl cyanoacetate was used in this reaction.

^c The catalyst was added in portions.

^d A number of cyanoacetic esters were used.

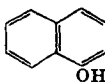
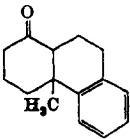
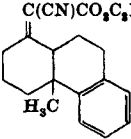
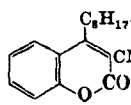
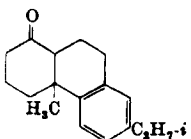
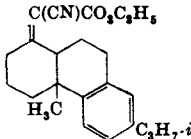
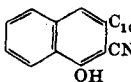
TABLE VII—Continued
CONDENSATIONS USING CYANOACETIC ESTERS

408

ORGANIC REACTIONS

THE KNOEVENAGEL CONDENSATION

407

C. Aromatic Aldehydes or Ketones—Continued				
Aldehyde or Ketone	Catalyst	Temperature	Product(s) and Yield(s) (%)	Refs.
Dibenzyl ketone	CH ₃ CO ₂ NH ₄	Boiling C ₆ H ₆	(C ₆ H ₅ CH ₂) ₂ C=C(CN)CO ₂ C ₂ H ₅ (—)	877-880
C ₆ H ₅ CH ₂ CH ₂ COC ₆ H ₅	Dowex 3 acetate CH ₃ CO ₂ NH ₄	" "	(C ₆ H ₅ CH ₂) ₂ C=C(CN)CO ₂ C ₂ H ₅ (35)	141
		160-180°	C ₆ H ₅ CH ₂ CH ₂ C(C ₆ H ₅)=C(CN)CO ₂ CH ₃ (38)	149
4-Methoxybenzyl phenyl ketone	"	170-180°	 C ₆ H ₄ OCH ₃ -4 ^b (10)	149
4-Benzoyloxyacetophenone	"	Boiling C ₆ H ₆	4-C ₆ H ₄ CH ₂ OC ₆ H ₄ C(CH ₃)=C(CN)CO ₂ R ¹ (—)	854
5-Phenyl-5,5-dicarbomethoxy-pentan-2-one	Piperidine, C ₆ H ₅ CH ₂ NH ₂ and CH ₃ CO ₂ H	" "	C ₆ H ₅ C(CO ₂ CH ₃) ₂ CH ₂ CH ₂ C(CH ₃)=C(CN)CO ₂ C ₂ H ₅ (62)	869
Phenyl 2-cyclohexylethyl ketone	CH ₃ CO ₂ NH ₄	" "	C ₆ H ₁₁ CH ₂ CH ₂ C(C ₆ H ₅)=C(CN)CO ₂ C ₂ H ₅ (75)	137
	" ^c	" "	 (72)	881
5-Anisyl-5-carbomethoxypentan-2-one	CH ₃ CONH ₂	—	4-CH ₃ OC ₆ H ₄ CH(CO ₂ C ₂ H ₅)CH ₂ CH ₂ -C(CH ₃)=C(CN)CO ₂ C ₂ H ₅ (—)	824, 1152
2-HOC ₆ H ₄ COC ₆ H _{17-n}	CH ₃ CO ₂ NH ₄ ^d	Boiling C ₆ H ₆	 C ₆ H _{17-n} ^b (40)	148
2-Hydroxy-5-methyloctanophenone	"	" "	2-HO-5-CH ₂ C ₆ H ₄ C(C ₆ H _{13-n})=C(CN)CO ₂ CH ₃ (—)	854
5-Anisyl-5-cyano-5-carbomethoxy-pentan-2-one	Piperidine, C ₆ H ₅ CH ₂ NH ₂ and CH ₃ CO ₂ H	" "	4-CH ₃ OC ₆ H ₄ C(CN)(CO ₂ C ₂ H ₅)CH ₂ -CH ₂ C(CH ₃)=C(CN)CO ₂ C ₂ H ₅ (76)	871
1-(2'-Methoxyphenyl)non-2-en-1-one	CH ₃ CO ₂ NH ₄	" "	n-C ₆ H ₁₃ CH=CHC(C ₆ H ₄ OCH ₃ -2)=C(CN)CO ₂ R ¹ (—)	854
11-Phenylundecapentaenal	Piperidine/C ₆ H ₅ OH	Room	C ₆ H ₅ (CH=CH) ₅ CH=C(CN)CO ₂ C ₂ H ₅ (—)	864
Diphenethyl ketone	CH ₃ CO ₂ NH ₄	Boiling C ₆ H ₆ or C ₆ H ₅ CH ₃	(C ₆ H ₅ CH ₂ CH ₂) ₂ C=C(CN)CO ₂ C ₂ H ₅ (73)	137, 815
4-n-Butylphenyl n-hexyl ketone	"	Boiling C ₆ H ₆	4-n-C ₆ H ₄ C ₆ H ₄ C(C ₆ H _{13-n})=C(CN)CO ₂ C ₂ H ₅ (35)	137
	" ^e	"	 (32)	1143
5-Anisyl-5,5-dicarbomethoxypentan-2-one	Piperidine, C ₆ H ₅ CH ₂ NH ₂ and CH ₃ CO ₂ H	" "	4-CH ₃ OC ₆ H ₄ C(CO ₂ C ₂ H ₅) ₂ CH ₂ -CH ₂ C(CH ₃)=C(CN)CO ₂ C ₂ H ₅ (88)	871
Phenyl 5-phenylpentyl ketone	CH ₃ CO ₂ NH ₄	" "	C ₆ H ₅ (CH ₂) ₅ C(C ₆ H ₅)=C(CN)CO ₂ C ₂ H ₅ (67)	137, 815
n-C ₁₁ H ₂₃ COC ₆ H ₅	CH ₃ CO ₂ NH ₄	Boiling C ₆ H ₆	n-C ₁₁ H ₂₃ C(C ₆ H ₅)=C(CN)CO ₂ C ₂ H ₅ (68)	137
Benzyl 1-naphthyl ketone	"	140-160°	No reaction	149
Benzyl 2-naphthyl ketone (crude)	"	"	 C ₁₀ H ₇ -2 (40) ^f	149

Note: References 285 to 1153 are on pp. 582-599.

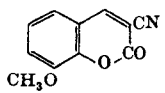
^b Ethyl cyanoacetate was used in this reaction.

^c The catalyst was added in portions.

^d The yield was calculated on the amount of benzyl 2-naphthyl ketone in the crude starting material.

^e A number of cyanoacetic esters were used.

TABLE VII—Continued
CONDENSATIONS USING CYANOACETIC ESTERS

C. Aromatic Aldehydes or Ketones—Continued				
Aldehyde or Ketone	Catalyst	Temperature	Product(s) and Yield(s) (%)	Refs.
	—	—	 (—)	882
4- <i>n</i> -C ₁₂ H ₂₅ OC ₆ H ₄ COCH ₃	CH ₃ CO ₂ NH ₄	Boiling C ₆ H ₆	4- <i>n</i> -C ₁₂ H ₂₅ OC ₆ H ₄ C(CH ₃)=C(CN)CO ₂ R ⁱ (—)	854
4-HOC ₆ H ₄ COC ₁₅ H ₃₁ · <i>n</i>	"	" "	4-HOC ₆ H ₄ C(C ₁₅ H ₃₁ · <i>n</i>)=C(CN)CO ₂ CH ₃ (—)	854
D. Aromatic Aldehydes or Ketones				
3,4-Cl ₂ C ₆ H ₃ CHO	Piperidine	—	3,4-Cl ₂ C ₆ H ₃ CH=C(CN)CO ₂ C ₂ H ₅ (—)	883
3-Nitro-4-chlorobenzaldehyde	"	Boiling <i>i</i> -C ₃ H ₇ OH	3-O ₂ N-4-ClC ₆ H ₃ CH=C(CN)CO ₂ C ₂ H ₅ (80)	884
2-Bromobenzaldehyde	Piperidine + C ₆ H ₅ CO ₂ H	Boiling C ₆ H ₆	2-BrC ₆ H ₄ CH=C(CN)CO ₂ C ₂ H ₅ (91)	155
4-Bromobenzaldehyde	Piperidine	Boiling C ₂ H ₅ OH	4-BrC ₆ H ₄ CH=C(CN)CO ₂ C ₂ H ₅ (60)	55
2-Chlorobenzaldehyde	"	Room	2-ClC ₆ H ₄ CH=C(CN)CO ₂ C ₂ H ₅ (70)	857, 885
4-Chlorobenzaldehyde	Piperidine/C ₂ H ₅ OH	65°	4-ClC ₆ H ₄ CH(CO ₂ H)CH ₂ CO ₂ H ^r (76)	848
2-Nitrobenzaldehyde	Piperidine/dioxane	Room	2-O ₂ NC ₆ H ₄ CH=C(CN)CO ₂ C ₂ H ₅ (68)	857
3-Nitrobenzaldehyde	Piperidine/C ₂ H ₅ OH	—	3-O ₂ NC ₆ H ₄ CH=C(CN)CO ₂ C ₂ H ₅ (—)	770
Benzaldehyde	Piperidine	Temperature allowed to rise	C ₆ H ₅ CH=C(CN)CO ₂ C ₂ H ₅ (80)	154, 856, 885
	Pyridine	—	C ₆ H ₅ CH=C(CN)CO ₂ C ₂ H ₅ (—)	156
	Piperidinium acetate + Pd/C and H ₂	60°	C ₆ H ₅ CH ₂ CH(CN)CO ₂ C ₂ H ₅ (63)	150
	Piperidine + <i>n</i> -C ₆ H ₁₁ CO ₂ H	Boiling C ₆ H ₆	C ₆ H ₅ CH=C(CN)CO ₂ C ₂ H ₅ (72)	69
Salicylaldehyde	Weak base resins	100°	C ₆ H ₅ CH=C(CN)CO ₂ C ₂ H ₅ (80)	675
	Piperidine	Cold	2-HOC ₆ H ₄ CH(CH(CN)CO ₂ C ₂ H ₅) ₂ (—)	170
	—	—	2-HOC ₆ H ₄ CH=C(CN)CO ₂ C ₂ H ₅ (<i>cis</i>) (—)	147
4-HOC ₆ H ₄ CHO	Piperidine/dioxane	Room	4-HOC ₆ H ₄ CH=C(CN)CO ₂ C ₂ H ₅ (58)	857
3,4-(HO) ₂ C ₆ H ₃ CHO (protocatechuic aldehyde)	Piperidine	Water bath	3,4-(HO) ₂ C ₆ H ₃ CH=C(CN)CO ₂ C ₂ H ₅ (Quant.)	886
Terephthalaldehyde	Piperidine/C ₂ H ₅ OH	Room	C ₆ H ₄ [CH=C(CN)CO ₂ C ₂ H ₅] ₂ -1,4 (96)	191, 697
3,4-Methylenedioxy benzaldehyde (piperonal)	Piperidine/dioxane	Room	3,4-(CH ₂ O) ₂ C ₆ H ₃ CH=C(CN)CO ₂ C ₂ H ₅ (77)	857
4-Hydroxyisophthalaldehyde	Piperidine + pyridine	Water bath	 CH=C(CN)CO ₂ C ₂ H ₅ (—)	491
2-Hydroxy-4,5-methylene dioxybenzaldehyde	Piperidine	Boiling C ₆ H ₅ OH	 (38) ^a	419
3-Bromo-6-methoxybenzaldehyde	CH ₃ CO ₂ NH ₄	Boiling C ₆ H ₆	3-Br-6-CH ₃ OC ₆ H ₃ CH=C(CN)CO ₂ C ₂ H ₅ (91)	888
	Piperidine/C ₂ H ₅ OH	Warm	3-Br-6-CH ₃ OC ₆ H ₃ CH=C(CN)CO ₂ C ₂ H ₅ (90)	110
3-Chloro-4-methoxybenzaldehyde	Piperidine	—	3-Cl-4-CH ₃ OC ₆ H ₃ CH=C(CN)CO ₂ C ₂ H ₅ (—)	883
3-Chloro-6-methoxybenzaldehyde	"	—	3-Cl-6-CH ₃ OC ₆ H ₃ CH=C(CN)CO ₂ C ₂ H ₅ (—)	883
4-Methylbenzaldehyde	CH ₃ CO ₂ NH ₄	Boiling C ₆ H ₆	4-CH ₃ C ₆ H ₄ CH=C(CN)CO ₂ C ₂ H ₅ (—)	756
2-Methoxybenzaldehyde	Piperidine	Reflux or room	2-CH ₃ OC ₆ H ₄ CH=C(CN)CO ₂ C ₂ H ₅ (86)	110, 490, 885
4-Methoxybenzaldehyde (anisaldehyde)	"	Room	4-CH ₃ OC ₆ H ₄ CH=C(CN)CO ₂ C ₂ H ₅ (79)	885
	Piperidinium acetate	120–130°	4-CH ₃ OC ₆ H ₄ CH=C(CN)CO ₂ C ₂ H ₅ (Quant.)	889
	CH ₃ CO ₂ NH ₄	Boiling C ₆ H ₆	4-CH ₃ OC ₆ H ₄ CH=C(CN)CO ₂ C ₂ H ₅ (—)	756
2-Hydroxy-3-methoxybenzaldehyde	Piperidine	Boiling C ₂ H ₅ OH	 (35)	146, 147
3-Methoxy-4-hydroxybenzaldehyde (vanillin)	Piperidine	Room or water bath	3-CH ₃ O-4-HOC ₆ H ₃ CH=C(CN)CO ₂ C ₂ H ₅ (100)	857, 886

Note: References 285 to 1153 are on pp. 582–599.

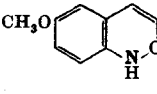
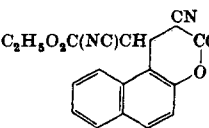
^a Ethyl cyanoacetate was used in this reaction.

ⁱ A number of cyanoacetic esters were used.

^r Methyl cyanoacetate was used in the condensation. The crude product was treated with potassium cyanide and then hydrolyzed.

^a The crude nitrile produced in the reaction was hydrolyzed.

TABLE VII—Continued
CONDENSATIONS USING CYANOACETIC ESTERS

D. Aromatic Aldehydes or Ketones—Continued				
Aldehyde or Ketone	Catalyst	Temperature	Product(s) and Yield(s) (%)	Refs.
4-CH ₃ NHC ₆ H ₄ CHO	Piperidine "	90–100° "	4-CH ₃ NHC ₆ H ₄ CH=C(CN)CO ₂ CH ₂ CH ₂ OH (—) 890 4-CH ₃ NHC ₆ H ₄ CH=C(CN)CO ₂ H-CH ₂ CHOHCH ₂ OH (—) 890	
2-Amino-3-methoxybenzaldehyde	"	Boiling C ₂ H ₅ OH	 (—) 85	
2-Amino-5-methoxybenzaldehyde	Pyridine	" "	 (—) 113	
4-Methoxyisophthalaldehyde	Piperidine + pyridine	Room	1-CH ₃ OC ₆ H ₄ [CH=C(CN)CO ₂ C ₂ H ₅] ₂ -2,4 (—) 491	
2,3-Dimethoxy-5-bromobenzaldehyde	CH ₃ CO ₂ NH ₂	Boiling C ₆ H ₆	2,3-(CH ₃ O) ₂ -5-BrC ₆ H ₃ CH=C(CN)CO ₂ C ₂ H ₅ (77–79) 891	
2,4-Dimethoxybenzaldehyde	Piperidine/C ₂ H ₅ OH	Room	2,4-(CH ₃ O) ₂ C ₆ H ₃ CH=C(CN)CO ₂ C ₂ H ₅ (—) 769	
2,5-Dimethoxybenzaldehyde	"	Room or 60°	2,5-(CH ₃ O) ₂ C ₆ H ₃ CH=C(CN)CO ₂ C ₂ H ₅ (95) 770, 892	
3,4-Dimethoxybenzaldehyde (veratraldehyde)	"	Room	3,4-(CH ₃ O) ₂ C ₆ H ₃ CH=C(CN)CO ₂ C ₂ H ₅ (Quant.) 769	
4-(CH ₃) ₂ NC ₆ H ₄ CHO	Piperidine	130°	4-(CH ₃) ₂ NC ₆ H ₄ CH=C(CN)CO ₂ C ₂ H ₅ (—) 893	
	Piperidinium acetate	Boiling C ₂ H ₅ OH	4-(CH ₃) ₂ NC ₆ H ₄ CH=C(CN)CO ₂ C ₂ H ₅ (—) 894	
	" "	" "	4-(CH ₃) ₂ NC ₆ H ₄ CH=C(CN)CO ₂ CH ₃ (48) 762, 894	
	Piperidine	90–100°	4-(CH ₃) ₂ NC ₆ H ₄ CH=C(CN)CO ₂ CH ₂ CH ₂ OH (—) 890	
	Piperidinium acetate	Boiling C ₂ H ₅ OH	4-(CH ₃) ₂ NC ₆ H ₄ CH=C(CN)CO ₂ CH ₂ CH ₂ OH (85) 762, 894	
	" "	" "	4-(CH ₃) ₂ NC ₆ H ₄ CH=C(CN)CO ₂ CH ₂ CH ₂ C ₆ H ₅ (83) 762	
4-C ₆ H ₄ NHC ₆ H ₄ CHO	Piperidine	90–100°	4-C ₆ H ₄ NHC ₆ H ₄ CH=C(CN)CO ₂ CH ₂ CH ₂ OH (—) 890	
2,5-Dimethoxyterephthalaldehyde	"	Boiling ethanol	2,5-(CH ₃ O) ₂ C ₆ H ₃ [CH=C(CN)CO ₂ C ₂ H ₅] ₂ -1,4 (—) 895	
6-Dimethylaminofulvene-2,3-dicarboxaldehyde	Piperidine/C ₂ H ₅ OH	Room	C ₆ H ₅ O ₂ C(NC)C=CH  CHN(CH ₃) ₂ (30) 711	
2-Isopropoxybenzaldehyde	"	"	2-i-C ₃ H ₇ OC ₆ H ₄ CH=C(CN)CO ₂ C ₂ H ₅ (65) 490	
2-Methyl-4,5-dimethoxybenzaldehyde	"	"	2-CH ₃ -4,5-(CH ₃ O) ₂ C ₆ H ₃ CH=C(CN)CO ₂ C ₂ H ₅ (98) 896	
2,4,5-Trimethoxybenzaldehyde	"	Room or 60°	2,4,5-(CH ₃ O) ₃ C ₆ H ₂ CH=C(CN)CO ₂ C ₂ H ₅ (98) 892, 897	
4-Methyl-(2'-chloroethyl)-aminobenzaldehyde	Piperidine	Boiling C ₂ H ₅ OH	4-CH ₃ (ClCH ₂ CH ₂)NC ₆ H ₄ CH=C(CN)CO ₂ C ₂ H ₅ (92) 898	
2-Methyl-4-dimethylaminobenzaldehyde	Piperidinium acetate	" "	2-CH ₃ -4-(CH ₃) ₂ NC ₆ H ₃ CH=C(CN)CO ₂ C ₂ H ₅ (66) 762, 894	
4-CH ₃ (C ₂ H ₅)NC ₆ H ₄ CHO	Piperidine	90–100°	4-CH ₃ (C ₂ H ₅)NC ₆ H ₄ CH=C(CN)CO ₂ CH ₂ CH ₂ OH (—) 890	
4-Methyl-(2'-hydroxyethyl)-aminobenzaldehyde ^a	"	"	4-CH ₃ (HOCH ₂ CH ₂)NC ₆ H ₄ CH=C(CN)CO ₂ -CH ₂ CH ₂ OH (—) 890	
1-Naphthaldehyde	Piperidinium benzoate	Boiling C ₄ H ₄	1-C ₁₀ H ₇ CH=C(CN)CO ₂ C ₂ H ₅ (93) 97	
	Morpholine	" "	1-C ₁₀ H ₇ CH=C(CN)CO ₂ C ₂ H ₅ (74) 899	
2-Naphthaldehyde	"	Gentle heat	2-C ₁₀ H ₇ CH=C(CN)CO ₂ C ₂ H ₅ (Quant.) 507	
	Piperidine	Boiling C ₂ H ₅ OH	2-C ₁₀ H ₇ CH=C(CN)CO ₂ C ₂ H ₅ (58) 713	
Azulene-1-carboxaldehyde	(C ₂ H ₅) ₃ NH/C ₂ H ₅ OH	Room	 CH=C(CN)CO ₂ C ₂ H ₅ (96) 568	
2-Hydroxy-1-naphthaldehyde	Piperidine	"	 (80) 81	

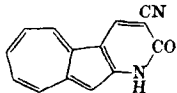
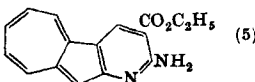
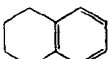
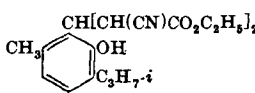
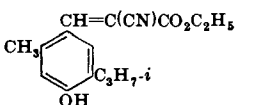

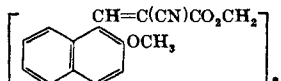
Note: References 285 to 1153 are on pp. 582–599.

^a Ethyl cyanoacetate was used in this reaction.

^b A similar product is reported using tetrahydrofurfuryl cyanoacetate.

^c The Schiff base with metanilic acid was used.

TABLE VII—Continued
CONDENSATIONS USING CYANOACETIC ESTERS

D. Aromatic Aldehydes or Ketones—Continued				
Aldehyde or Ketone	Catalyst	Temperature	Product(s) and Yield(s) (%)	Refs.
2-Aminoazulene-1-carboxaldehyde	Piperidine	Boiling C_2H_5OH	 (18)	717, 718
			 (5)	
Ferrocenecarboxaldehyde	Piperidine/ C_2H_5OH	Room	$C_2H_5FeC_5H_4CH=C(CN)CO_2C_2H_5$ (58)	900
	Piperidinium acetate	Boiling C_6H_6	$C_5H_5FeC_5H_4CH=C(CN)CO_2C_2H_5$ (84)	900
5,6,7,8-Tetrahydronaphthalene-2-carboxaldehyde	Piperidine	Steam bath	 $CH(CO_2H)CH_2CO_2H$ (60)	713
4-Methyl-(2'-cyanoethyl)aminobenzaldehyde	Piperidinium acetate	Boiling C_2H_5OH	4- $CH_3(CNCH_2CH_2)NC_6H_4CH=C(CN)CO_2CH_3$ (48)	762
	" "	" "	4- $CH_3(CNCH_2CH_2)NC_6H_4CH=C(CN)CO_2CH_2C_6H_5$ (78)	762, 894
	" "	" "	4- $CH_3(CNCH_2CH_2)NC_6H_4CH=C(CN)CO_2CH_2CH_2C_6H_5$ (78)	762
4-Di-(2'-chloroethyl)aminobenzaldehyde	Piperidine/dioxane	Room	4-($ClCH_2CH_2$) $_2NC_6H_4CH=C(CN)CO_2C_2H_5$ (89)	273, 857
	Piperidine	90–100°	4-($ClCH_2CH_2$) $_2NC_6H_4CH=C(CN)CO_2CH_2CH_2OH$ (—)	890
	Piperidine/dioxane	Room	4-($ClCH_2CH_2$) $_2NC_6H_4CH=C(CN)CO_2CH_3$ (88)	278
2-Hydroxy-3-isopropyl-6-methylbenzaldehyde	Piperidinium acetate	Boiling C_2H_5OH	 (40)	83
4-Hydroxy-3-isopropyl-6-methylbenzaldehyde	Piperidinium acetate/ C_2H_5OH	Room	 (—)	83
3,4-Diethoxybenzaldehyde	Piperidine/dioxane	"	3,4-(C_2H_5O) $_2C_6H_3CH=C(CN)CO_2C_2H_5$ (86)	857
2-Ethyl-4,5-dimethoxybenzaldehyde	Piperidine/ C_2H_5OH	"	2- C_2H_5 -4,5-(CH_3O) $_2C_6H_3CH=C(CN)CO_2C_2H_5$ (79)	1144
4-Ethyl-(2'-chloroethyl)aminobenzaldehyde	Piperidine	Boiling C_2H_5OH	4- $C_2H_5(ClCH_2CH_2)NC_6H_4CH=C(CN)CO_2C_2H_5$ (—)	898
2-Chloro-4-diethylaminobenzaldehyde	"	Boiling $i-C_3H_7OH$	2- Cl -4-(C_2H_5) $_2NC_6H_3CH=C(CN)CO_2C_2H_5$ (—)	901
	"	" "	2- Cl -4-(C_2H_5) $_2NC_6H_3CH=C(CN)CO_2CH_2CH_2CN$ (—)	901
4-Diethylaminobenzaldehyde	Piperidine/dioxane	Room	4-(C_2H_5) $_2NC_6H_4CH=C(CN)CO_2C_2H_5$ (81)	857
	Piperidine	Boiling $i-C_3H_7OH$	4-(C_2H_5) $_2NC_6H_4CH=C(CN)CO_2CH_2$  (46)	887
4-Ethyl(2'-hydroxyethyl)aminobenzaldehyde ^a	"	90–100°	4- $C_2H_5(HOCH_2CH_2)NC_6H_4CH=C(CN)CO_2CH_2CH_2OH$ (—)	890
4-Methyl(2'-methoxyethyl)aminobenzaldehyde	"	90–100°	4- $CH_3(CH_3OCH_2CH_2)NC_6H_4CH=C(CN)CO_2CH_2CH_2OH$ (—)	890
4-Di(2'-hydroxyethyl)aminobenzaldehyde ^a	"	90–100°	4-($HOCH_2CH_2$) $_2NC_6H_4CH=C(CN)CO_2CH_2CH_2OH$ (—)	890
2-Hydroxy-4-diethylaminobenzaldehyde	"	Boiling $i-C_3H_7OH$	2- HO -4-(C_2H_5) $_2NC_6H_3CH=CHCO_2C_2H_5$ (—)	901
6-Methoxy-2-naphthaldehyde	"	Boiling C_2H_5OH	6- $CH_3OC_10H_6CH=C(CN)CO_2C_2H_5$ -2 (65)	713
2-Methoxy-1-naphthaldehyde	"	95°	2- $CH_3OC_10H_6CH=C(CN)CO_2CH_2CH_2CN$ -1 (—)	902, 903
	Pyridine	Boiling C_2H_5OH	 (—)	902, 903

Note: References 285 to 1153 are on pp. 582–599.

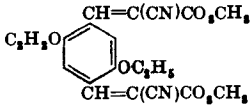
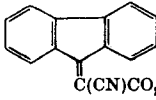
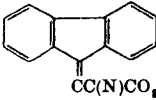
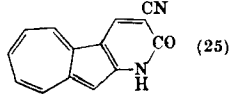
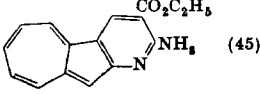
^a The Schiff base with metanilic acid was used.

^b This product was isolated after addition of hydrogen cyanide and hydrolysis.

TABLE VII—Continued
CONDENSATIONS USING CYANOACETIC ESTERS

414

ORGANIC REACTIONS

D. Aromatic Aldehydes or Ketones—Continued				
Aldehyde or Ketone	Catalyst	Temperature	Product(s) and Yield(s) (%)	Refs.
2-Methoxy-4-diethylaminobenzaldehyde	Piperidine	Boiling isopropyl alcohol	2-CH ₃ O-4-(C ₂ H ₅) ₂ NC ₆ H ₃ CH=C(CN)CO ₂ C ₂ H ₅ (—)	901
4-Ethyl-(2'-methoxyethyl)-aminobenzaldehyde	"	90–100°	4-C ₂ H ₅ (CH ₃ OCH ₂ CH ₂)NC ₆ H ₄ CH=C(CN)CO ₂ CH ₂ CH ₂ OH (—)	890
2,5-Diethoxyterephthalaldehyde	"	Boiling C ₂ H ₅ OH	 (—)	895
Fluorenone	CH ₃ CO ₂ NH ₄ ^a	Boiling C ₆ H ₆	 (87)	137, 815
	CH ₃ CO ₂ NH ₄ + CH ₃ CONH ₂	140°	 (60)	904
2,4'-Dichlorobenzophenone	CH ₃ CO ₂ NH ₄ ^a	Boiling C ₆ H ₆	2-ClC ₆ H ₄ C(C ₆ H ₄ Cl-4')=C(CN)CO ₂ C ₂ H ₅ (46)	137, 815
4,4'-Dichlorobenzophenone	"	" "	(4-ClC ₆ H ₄) ₂ C=C(CN)CO ₂ C ₂ H ₅ (43)	137
4-Chlorobenzophenone	"	" "	(4-ClC ₆ H ₄)C(C ₆ H ₅)=C(CN)CO ₂ C ₂ H ₅ (82)	137
Benzophenone	"	" "	(C ₆ H ₅) ₂ C=C(CN)CO ₂ C ₂ H ₅ (68)	47
	"	" "	(C ₆ H ₅) ₂ C=C(CN)CO ₂ C ₂ H ₅ (84)	137, 815
	CH ₃ CO ₂ NH ₄ + CH ₃ CONH ₂	140°	(C ₆ H ₅) ₂ C=C(CN)CO ₂ C ₂ H ₅ (33)	904
	ε-Aminocaproic acid + CH ₃ CO ₂ H	Boiling C ₆ H ₆	(C ₆ H ₅) ₂ C=C(CN)CO ₂ C ₂ H ₅ (55)	106
Benzophenone imine	None	70°	(C ₆ H ₅) ₂ C=C(CN)CO ₂ C ₂ H ₅ (—)	32, 164
2-Acetamidoazulene-1-carboxaldehyde	Piperidine	Boiling C ₂ H ₅ OH	 (25)	717, 718
	"	"	 (45)	
2-Ethoxy-1-naphthaldehyde	"	95°	2-C ₂ H ₅ OC ₁₀ H ₇ CH=C(CN)CO ₂ C ₂ H ₅ -1 ^w (95)	902, 903
4-Dimethylamino-1-naphthaldehyde	"	Boiling C ₂ H ₅ OH	4-(CH ₃) ₂ NC ₁₀ H ₇ CH=C(CN)CO ₂ C ₂ H ₅ -1 (95)	905
4-Di-(2'-cyanoethyl)aminobenzaldehyde	Piperidinium acetate	" "	4-(NCCH ₂ CH ₂) ₂ NC ₆ H ₄ CH=C(CN)CO ₂ CH ₃ (65)	762
	Piperidine	Water bath	4-(NCCH ₂ CH ₂) ₂ NC ₆ H ₄ CH=C(CN)CO ₂ C ₂ H ₅ (91)	533
	Piperidinium acetate	Boiling C ₂ H ₅ OH	4-(NCCH ₂ CH ₂) ₂ NC ₆ H ₄ CH=C(CN)-CO ₂ CH ₂ C ₆ H ₅ (83)	762, 894
2-Ethoxy-4-diethylaminobenzaldehyde	Piperidine	Boiling i-C ₃ H ₇ OH	2-C ₂ H ₅ O-4-(C ₂ H ₅) ₂ NC ₆ H ₃ CH=C(CN)CO ₂ C ₂ H ₅ (57)	894
	"	" "	2-C ₂ H ₅ O-4-(C ₂ H ₅) ₂ NC ₆ H ₃ CH=C(CN)CO ₂ CH ₂ CH ₂ CN (—)	894
Benzil	(C ₂ H ₅) ₂ NH or piperidine	70°, then 100°	C ₆ H ₅ COC(C ₆ H ₅)=C(CN)CO ₂ C ₂ H ₅ (54)	906
Benzoylformanilide	Piperidine	Boiling C ₂ H ₅ OH	C ₆ H ₅ COC(C ₆ H ₅)=C(CN)CO ₂ C ₂ H ₅ (65)	907
	(C ₂ H ₅) ₂ NH	0°	C ₂₁ H ₂₃ O ₃ N ₃ (75–80)	163
	Piperidine	0°	C ₂₇ H ₂₉ O ₃ N ₃ (75–80)	
2-Methoxybenzophenone	CH ₃ CO ₂ NH ₄	Boiling C ₆ H ₆	2-CH ₃ OC ₆ H ₄ C(C ₆ H ₅)=C(CN)CO ₂ C ₂ H ₅ (—)	908
4-Methoxybenzophenone	"	" "	4-CH ₃ OC ₆ H ₄ C(C ₆ H ₅)=C(CN)CO ₂ C ₂ H ₅ (75)	137, 815
2-Allyloxy-1-naphthaldehyde	Piperidine	95°	2-CH ₃ =CHCH ₂ OC ₁₀ H ₇ CH=C(CN)CO ₂ C ₂ H ₅ -1 (—)	902
4-Ethyl-(2'-carbethoxyethyl)-aminobenzaldehyde	"	Boiling i-C ₃ H ₇ OH	4-C ₂ H ₅ (C ₂ H ₅ O ₂ CCH ₂ CH ₂)NC ₆ H ₄ CH=C(CN)CO ₂ CH ₂ C ₆ H ₅ O ^z (85)	887

Note: References 285 to 1153 are on pp. 582–599.

^a The catalyst was added in portions.

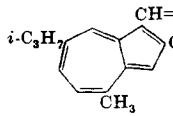
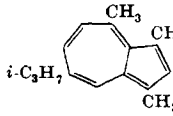
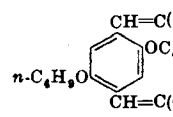
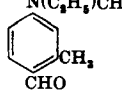
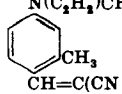
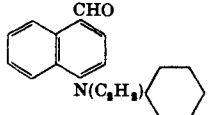
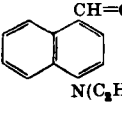
^w Other cyanoacetic esters were used, but no yields were given.

^z Tetrahydrofurfuryl cyanoacetate was used in this reaction.

THE KNOEVENAGEL CONDENSATION

415












TABLE VII—Continued
CONDENSATIONS USING CYANOACETIC ESTERS

D. Aromatic Aldehydes or Ketones—Continued				
Aldehyde or Ketone	Catalyst	Temperature	Product(s) and Yield(s) (%)	Refs.
$\text{CH}_3\text{N} \left[\text{C}_6\text{H}_4\text{CHO} \right]_2$	Piperidine	Boiling $i\text{-C}_3\text{H}_7\text{OH}$	$\text{CH}_3\text{N} \left[\text{C}_6\text{H}_4\text{CH}=\text{C}(\text{CN})\text{CO}_2\text{C}_2\text{H}_5 \right]_2$ (80)	909
	"	" "	$\text{CH}_3\text{N} \left[\text{C}_6\text{H}_4\text{CH}=\text{C}(\text{CN})\text{CO}_2\text{CH}_2\text{CH}_2\text{CN} \right]_2$ (99)	909
	"	" "	$\text{CH}_3\text{N} \left[\text{C}_6\text{H}_4\text{CH}=\text{C}(\text{CN})\text{CO}_2\text{CH}_2\text{C}_4\text{H}_7\text{O} \right]_2^x$ (100)	887
	"	" "	$\text{CH}_3\text{N} \left[\text{C}_6\text{H}_4\text{CH}=\text{C}(\text{CN})\text{CO}_2 \text{ (furan ring)} \right]_2$ (100)	909
3-Methoxy-4-benzyloxybenzaldehyde	$\text{CH}_3\text{NH}_2\text{Cl} + \text{Na}_2\text{CO}_3$	Warm	$3\text{-CH}_3\text{O}-4\text{-C}_6\text{H}_5\text{CH}_2\text{OC}_6\text{H}_5\text{CH}=\text{C}(\text{CN})\text{CO}_2\text{C}_2\text{H}_5$ (Quant.)	910
3,5-Di- i -butyl-4-hydroxybenzaldehyde	Pyridine, $\text{CH}_3\text{CO}_2\text{H}$ and $(\text{CH}_3\text{CO})_2\text{O}$	B.p.	$3,5\text{-}(i\text{-C}_4\text{H}_9)_2\text{-4-HOC}_6\text{H}_3\text{CH}=\text{C}(\text{CN})\text{CO}_2\text{C}_2\text{H}_5$ (—)	724
4- n -Butyl-isobutylaminobenzaldehyde	Piperidine	Boiling $\text{C}_2\text{H}_5\text{OH}$	$4\text{-}n\text{-C}_4\text{H}_9(i\text{-C}_4\text{H}_9)\text{NC}_6\text{H}_4\text{CH}=\text{C}(\text{CN})\text{CO}_2\text{C}_2\text{H}_5$ (—)	240, 773
4-Methyl-isooheptylaminobenzaldehyde	"	" "	$4\text{-CH}_3(i\text{-C}_7\text{H}_{15})\text{NC}_6\text{H}_4\text{CH}=\text{C}(\text{CN})\text{CO}_2\text{CH}_3$ (—)	240
2,4-Dimethyl-7-isopropylazulene-1-carboxaldehyde	$(\text{C}_2\text{H}_5)_2\text{NH}/\text{C}_2\text{H}_5\text{OH}$	Room	 (84)	568
3,8-Dimethyl-5-isopropylazulene-1-carboxaldehyde	"	"	 (93)	568
2,5-Dibutoxyterephthalaldehyde	Piperidine	Boiling $\text{C}_2\text{H}_5\text{OH}$	 (—)	895
2-Chloro-4-di-(2'-carbethoxyethyl)-aminobenzaldehyde	"	Boiling $i\text{-C}_3\text{H}_7\text{OH}$	$2\text{-Cl-4-(C}_6\text{H}_5\text{O}_2\text{CCH}_2\text{CH}_2)_2\text{NC}_6\text{H}_3\text{CH}=\text{C}(\text{CN})\text{CO}_2\text{C}_2\text{H}_5$ (—)	901
	"	Boiling CHCl_3	$2\text{-Cl-4-(C}_6\text{H}_5\text{O}_2\text{CCH}_2\text{CH}_2)_2\text{NC}_6\text{H}_3\text{CH}=\text{C}(\text{CN})\text{CO}_2\text{CH}_2\text{C}_4\text{H}_7\text{O}^x$ (—)	887
4-Di-(2'-carbethoxyethyl)-aminobenzaldehyde	"	Boiling $i\text{-C}_3\text{H}_7\text{OH}$	$4\text{-(C}_6\text{H}_5\text{O}_2\text{CCH}_2\text{CH}_2)_2\text{NC}_6\text{H}_4\text{CH}=\text{C}(\text{CN})\text{CO}_2\text{C}_2\text{H}_5$ (—)	901
	"	Boiling CHCl_3	$4\text{-(C}_6\text{H}_5\text{O}_2\text{CCH}_2\text{CH}_2)_2\text{NC}_6\text{H}_4\text{CH}=\text{C}(\text{CN})\text{CO}_2\text{CH}_2\text{C}_4\text{H}_7\text{O}^x$ (87)	887
$4\text{-C}_6\text{H}_5\text{NHCO}_2\text{CH}_2\text{CH}_2\text{N(C}_6\text{H}_5)_2\text{-C}_6\text{H}_5\text{CHO}$	Piperidine/ CH_3OH	—	$4\text{-C}_6\text{H}_5\text{NHCO}_2\text{CH}_2\text{CH}_2\text{N(C}_6\text{H}_5)_2\text{C}_6\text{H}_4\text{CH}=\text{C}(\text{CN})\text{CO}_2\text{CH}_3$ (—)	774
2-Methyl-4-di-(2'-carbethoxyethyl)-aminobenzaldehyde	Piperidine	Boiling $i\text{-C}_3\text{H}_7\text{OH}$	$2\text{-CH}_3\text{-4-(C}_6\text{H}_5\text{O}_2\text{CCH}_2\text{CH}_2)_2\text{NC}_6\text{H}_3\text{CH}=\text{C}(\text{CN})\text{CO}_2\text{C}_2\text{H}_5$ (—)	901
	"	Boiling CHCl_3	$2\text{-CH}_3\text{-4-(C}_6\text{H}_5\text{O}_2\text{CCH}_2\text{CH}_2)_2\text{NC}_6\text{H}_3\text{CH}=\text{C}(\text{CN})\text{CO}_2\text{CH}_2\text{C}_4\text{H}_7\text{O}^x$ (—)	887
4- n -Butyl(isooheptyl)aminobenzaldehyde	"	Boiling CH_3OH	$4\text{-}n\text{-C}_4\text{H}_9(i\text{-C}_7\text{H}_{15})\text{NC}_6\text{H}_4\text{CH}=\text{C}(\text{CN})\text{CO}_2\text{CH}_3$ (—)	773
$\text{N(C}_6\text{H}_5)_2\text{CH}_2\text{CH}_2\text{OCONHC}_6\text{H}_5$ 	Piperidine/ CH_3OH	—	 (—)	774
 $\text{N(C}_6\text{H}_5)_2$	Piperidine/ $\text{C}_2\text{H}_5\text{OH}$	—	 (—)	905
4-Di- n -butylamino-1-naphthaldehyde	"	—	$4\text{-(}n\text{-C}_4\text{H}_9)_2\text{NC}_{10}\text{H}_7\text{CH}=\text{C}(\text{CN})\text{CO}_2\text{C}_2\text{H}_5$ (—)	905

Note: References 285 to 1153 are on pp. 582-599.

* Tetrahydrofurfuryl cyanoacetate was used in this reaction.

TABLE VII—Continued
CONDENSATIONS USING CYANOACETIC ESTERS

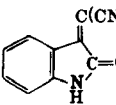
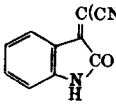
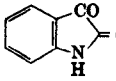
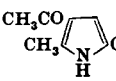
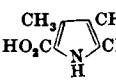
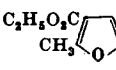
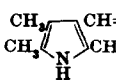
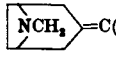
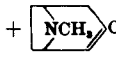

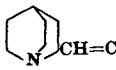
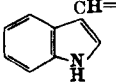
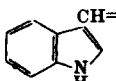
D. Aromatic Aldehydes or Ketones—Continued				
Aldehyde or Ketone	Catalyst	Temperature	Product(s) and Yield(s) (%)	Refs.
$\text{N} \left[\text{C}_6\text{H}_4\text{CHO} \right]_3$	Piperidine	Boiling $\text{C}_2\text{H}_5\text{OH}$	$\text{N} \left[\text{C}_6\text{H}_4\text{CH}=\text{C}(\text{CN})\text{CO}_2\text{C}_2\text{H}_5 \right]_3$ (95)	909
E. Heterocyclic Aldehydes or Ketones				
Glycidaldehyde	Piperidinium acetate	38°	 $\text{CH}=\text{C}(\text{CN})\text{CO}_2\text{C}_2\text{H}_5$ (79)	175
4,5-Dichlorothiophene-2-carboxaldehyde	Piperidine	−2° to −5°	 $\text{CH}=\text{C}(\text{CN})\text{CO}_2\text{C}_2\text{H}_5$ (80)	578
Furfural	Weak base resins	100°	$2\text{-C}_4\text{H}_3\text{OCH}=\text{C}(\text{CN})\text{CO}_2\text{C}_2\text{H}_5$ Poor + $2\text{-C}_4\text{H}_3\text{OCH}[\text{CH}(\text{CN})\text{CO}_2\text{C}_2\text{H}_5]_2$ (—)	675
Thiophene-2-carboxaldehyde	Piperidine/dioxane	Room	$2\text{-C}_4\text{H}_3\text{OCH}=\text{C}(\text{CN})\text{CO}_2\text{C}_2\text{H}_5$ (88)	246
Pyridine-2-carboxaldehyde	Piperidine/ $\text{C}_2\text{H}_5\text{OH}$	"	$2\text{-C}_4\text{H}_3\text{SCH}=\text{C}(\text{CN})\text{CO}_2\text{C}_2\text{H}_5$ (93)	96, 246
Pyridine-3-carboxaldehyde	$(\text{C}_2\text{H}_5)_2\text{NH}$	"	$2\text{-C}_5\text{H}_4\text{NCH}=\text{C}(\text{CN})\text{CO}_2\text{C}_2\text{H}_5$ (87)	911
Pyridine-4-carboxaldehyde	Piperidinium acetate	Boiling $\text{C}_2\text{H}_5\text{OH}$	$3\text{-C}_5\text{H}_4\text{NCH}=\text{C}(\text{CN})\text{CO}_2\text{C}_2\text{H}_5$ (—)	190
	$(\text{C}_2\text{H}_5)_2\text{NH}$	Room	$3\text{-C}_5\text{H}_4\text{NCH}=\text{C}(\text{CN})\text{CO}_2\text{CH}_2\text{C}_6\text{H}_5$ (77)	762
	Piperidinium acetate	Boiling $\text{C}_2\text{H}_5\text{OH}$	$4\text{-C}_5\text{H}_4\text{NCH}=\text{C}(\text{CN})\text{CO}_2\text{C}_2\text{H}_5$ (—)	190
	$\text{CH}_3\text{CO}_2\text{NH}_2$	Boiling CHCl_3	$4\text{-C}_5\text{H}_4\text{NCH}=\text{C}(\text{CN})\text{CO}_2\text{CH}_2\text{C}_6\text{H}_5$ (62)	762
2-Acetylthiophene			$2\text{-C}_4\text{H}_3\text{SC}(\text{CH}_3)=\text{C}(\text{CN})\text{CO}_2\text{CH}_3$ (—)	809
1-Methyl-4-piperidone	"	Boiling C_6H_6	 $\text{C}(\text{CN})\text{CO}_2\text{C}_2\text{H}_5$ (96)	776
	$\text{CH}_3\text{CO}_2\text{NH}_4$ + Pd/C and H_2	50–60°	 $\text{CH}(\text{CN})\text{CO}_2\text{C}_2\text{H}_5$ (82)	151
4-Carboxy-5-methylfurfural	$(\text{C}_2\text{H}_5)_2\text{NH}/\text{C}_2\text{H}_5\text{OH}$	0°, then room	 $\text{CH}=\text{C}(\text{CN})\text{CO}_2\text{C}_2\text{H}_5$ (75)	777
β -(2-Thienyl)acrolein	CH_3CONH_2	Boiling $\text{CH}_3\text{CO}_2\text{H}$	$2\text{-C}_4\text{H}_3\text{SCH}=\text{CHCH}=\text{C}(\text{CN})\text{CO}_2\text{C}_2\text{H}_5$ (90)	184
3,4-Dimethylpyrrole-2-carboxaldehyde	$\text{CH}_3\text{NH}_2/\text{C}_2\text{H}_5\text{OH}$	Water bath	 $\text{CH}=\text{C}(\text{CN})\text{CO}_2\text{CH}_3$ (98)	778
3,5-Dimethylpyrrole-2-carboxaldehyde	$\text{C}_6\text{H}_5\text{NH}_2$	—	 $\text{CH}=\text{C}(\text{CN})\text{CO}_2\text{C}_2\text{H}_5$ (70)	912
2,4-Dimethylpyrrole-3-carboxaldehyde	$\text{CH}_3\text{NH}_2\text{Cl} + \text{Na}_2\text{CO}_3$	Room	 $\text{CH}=\text{C}(\text{CN})\text{CO}_2\text{C}_2\text{H}_5$ (—)	913
3-Quinuclidone	$\text{CH}_3\text{CO}_2\text{NH}_4$	Boiling C_6H_6	 $\text{CH}(\text{CN})\text{CO}_2\text{C}_2\text{H}_5$ (70)	615
2,5-Dimethyltetrahydrothiapyran-4-one	"	" "	 $\text{C}(\text{CN})\text{CO}_2\text{C}_2\text{H}_5$ (75)	914
Isatin	Piperidine	Boiling $\text{C}_2\text{H}_5\text{OH}$	 $\text{C}(\text{CN})\text{CO}_2\text{C}_2\text{H}_5$ (73)	915, 916

Note: References 285 to 1153 are on pp. 582–599.

TABLE VII—Continued
CONDENSATIONS USING CYANOACETIC ESTERS

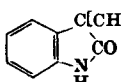
420

ORGANIC REACTIONS

<i>E. Heterocyclic Aldehydes or Ketones—Continued</i>				
Aldehyde or Ketone	Catalyst	Temperature	Product(s) and Yield(s) (%)	Refs.
Isatin (contd.)	Piperidine	Boiling C_2H_5OH	 $C(CN)CO_2C_2H_5$ ^{9,10} $C=C(CN)CO_2C_2H_5$ (—)	915
	$CH_3CO_2NH_4$	120–140°	 $C(CN)CO_2CH_3$ (88)	149
Isatin-2-anil	„	140–150°	 $C(CN)CO_2CH_3$ (65)	149
4-Acetyl-5-methylpyrrole-2-carboxaldehyde	$(C_2H_5)_2NH/C_2H_5OH$	Less than 10°	 CH_3CO CH_3 $CH=C(CN)CO_2C_2H_5$ (93)	780
5-Carboxy-2,4-dimethylpyrrole-3-carboxaldehyde	$C_2H_5NH_2/C_2H_5OH$	—	 CH_3 $CH=C(CN)CO_2C_2H_5$ (—)	918
4-Carboethoxy-5-methylfurfural	$(C_2H_5)_2NH/C_2H_5OH$	0°, then room	 $C_2H_5O_2C$ CH_3 $CH=C(CN)CO_2C_2H_5$ (Quant.)	777
2,4,5-Trimethylpyrrole-3-carboxaldehyde	$CH_3NH_2Cl + Na_2CO_3$	Room	 CH_3 $CH=C(CN)CO_2C_2H_5$ (—)	913
Tropinone	$CH_3CO_2NH_4$	Boiling C_2H_5	 NCH_3 $C=C(CN)CO_2C_2H_5$ (26)	151
			+  $CH(CN)CO_2C_2H_5$ (—)	
	$CH_3CO_2NH_4$ + Pd/C and H_2	50–60°	 $CH(CN)CO_2C_2H_5$ (64)	151
Quinuclidine-2-carboxaldehyde	Pyridine + piperidine	Room	 $CH=C(CN)CO_2C_2H_5$ (97)	919
Indole-3-carboxaldehyde	Piperidine	„	 $CH=C(CN)CO_2C_2H_5$ (94)	237, 246, 623
	„	Boiling C_2H_5OH	 $CH=C(CN)CO_2C_2H_5$ (98)	920

Note: References 285 to 1153 are on pp. 582–599.

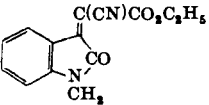
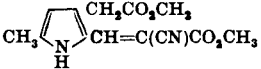
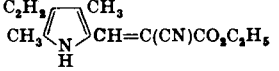
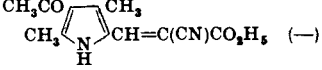
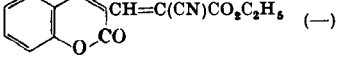
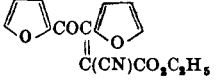
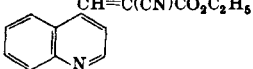
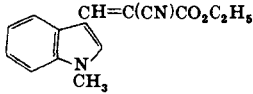
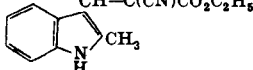
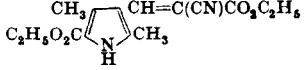
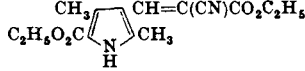
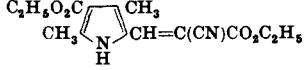
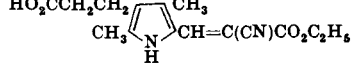
⁹ Cyanoacetic ester in 100% excess was used.

¹⁰ This compound has been shown to be  $C[CH(CN)CO_2C_2H_5]_2$ (ref. 917).

THE KNOEVENAGEL CONDENSATION

421

TABLE VII—Continued
CONDENSATIONS USING CYANOACETIC ESTERS

E. Heterocyclic Aldehydes or Ketones—Continued				
Aldehyde or Ketone	Catalyst	Temperature	Product(s) and Yield(s) (%)	Refs.
N-Methylisatin	Piperidine	Boiling C ₂ H ₅ OH	 (84)	916
Methyl 2-formyl-5-methyl-3-pyrrolacetate	CH ₃ NH ₂ Cl + Na ₂ CO ₃	Boiling alcohol	 (70)	912
3,5-Dimethyl-4-ethylpyrrole-2-carboxaldehyde	(C ₂ H ₅) ₂ NH	Room	 (Quant.)	643
3,5-Dimethyl-4-acetylpyrrole-2-carboxaldehyde	CH ₃ NH ₂ Cl + Na ₂ CO ₃	—	 (—)	913
Coumarin-3-carboxaldehyde	None	Room	 (—)	629
Furil	Piperidine	Boiling C ₂ H ₅ OH	 (—)	734
Quinoline-4-carboxaldehyde hydrate (cinchoninaldehyde)	Aqueous (C ₂ H ₅) ₂ NH	Room	 (90)	42
1-Methylindole-3-carboxaldehyde	Piperidine	„	 (94)	237, 623
2-Methylindole-3-carboxaldehyde	Piperidine/C ₂ H ₅ OH	„	 (26)	623
4-Carbethoxy-5-ethylfurfural	„ „	„	No reaction	777
2,4-Dimethyl-5-carbethoxypyrrole-3-carboxaldehyde	CH ₃ NH ₂ Cl + Na ₂ CO ₃	„	 (—)	913
	C ₆ H ₆ NH ₂	—	 (90-95)	918
3,5-Dimethyl-4-carbethoxypyrrole-2-carboxaldehyde	CH ₃ NH ₂ Cl + Na ₂ CO ₃	Room	 (Quant.)	913
β-(2,4-Dimethyl-5-formyl)-3-pyrrolpropionic acid	(C ₂ H ₅) ₂ NH	„	 (—)	643


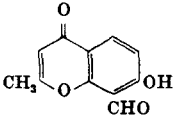
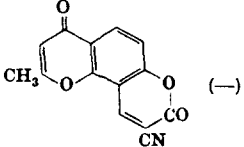
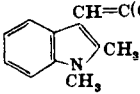
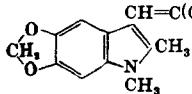



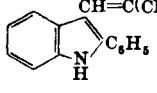
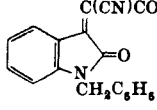
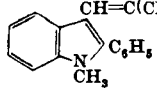
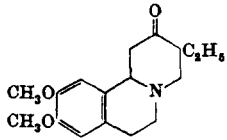
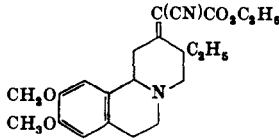
Note: References 285 to 1153 are on pp. 582-599.

TABLE VII—Continued
CONDENSATIONS USING CYANOACETIC ESTERS

424

ORGANIC REACTIONS

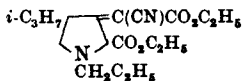
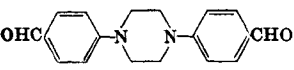
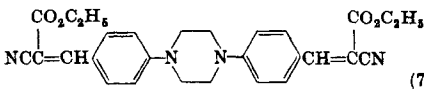
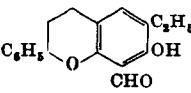
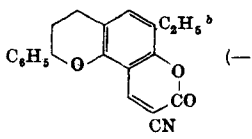
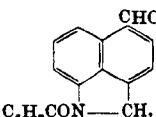
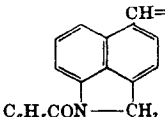
THE KNOEVENAGEL CONDENSATION

<i>E. Heterocyclic Aldehydes or Ketones—Continued</i>				
Aldehyde or Ketone	Catalyst	Temperature	Product(s) and Yield(s) (%)	Refs.
2-Benzoylthiophene	CH ₃ CO ₂ NH ₄	Boiling C ₆ H ₆	 C(C ₆ H ₅)=C(CN)CO ₂ C ₂ H ₅ (53)	137, 815
	Piperidine	—	 (—)	738
1,2-Dimethylindole-3-carboxaldehyde	Piperidine/C ₂ H ₅ OH	Room	 (37)	623
5,6-Methylenedioxy-1,2-dimethylindole-3-carboxaldehyde	CH ₃ CO ₂ NH ₄	Boiling C ₆ H ₆	 (83)	921
4-Carbethoxy-5-carbethoxymethylfurfural	Piperidine	—	No reaction	777
1-Benzyl-4-piperidone	CH ₃ CO ₂ NH ₄	Boiling C ₆ H ₆	C ₂ H ₅ CH ₂ N  =C(CN)CO ₂ C ₂ H ₅ (40)	922
4-Carbethoxy-5-phenylfurfural	(C ₂ H ₅) ₂ NH/C ₂ H ₅ OH	Room	C ₂ H ₅ O ₂ C  CH=C(CN)CO ₂ C ₂ H ₅ (85)	777
1-Benzoyl-3-ethyl-4-piperidone	CH ₃ CO ₂ NH ₄	Boiling C ₆ H ₆	C ₆ H ₅ CON  =C(CN)CO ₂ C ₂ H ₅ (80)	922
2-Phenylindole-3-carboxaldehyde	Piperidine + pyridine	Boiling i-C ₃ H ₇ OH	 CH=C(CN)CO ₂ C ₂ H ₅ (89)	923
1-Benzylisatin	Piperidine	Boiling C ₂ H ₅ OH	 C(CN)CO ₂ C ₂ H ₅ (75)	916
1-Methyl-2-phenylindole-3-carboxaldehyde	Piperidine + pyridine	Boiling i-C ₃ H ₇ OH	 CH=C(CN)CO ₂ C ₂ H ₅ (80)	924
	CH ₃ CO ₂ NH ₄	Boiling C ₆ H ₅ CH ₃	 C(CN)CO ₂ C ₂ H ₅ (66)	925, 114

Note: References 285 to 1153 are on pp. 582-599.

425

TABLE VII—*Continued*
 CONDENSATIONS USING CYANOACETIC ESTERS

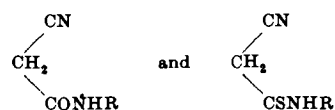
<i>E. Heterocyclic Aldehydes or Ketones—Continued</i>				
Aldehyde or Ketone	Catalyst	Temperature	Product(s) and Yield(s) (%)	Refs.
Ethyl 1-benzyl-4-isopropyl-3-pyrrolidone-2-carboxylate	$\text{CH}_3\text{CO}_2\text{NH}_4$	Boiling C_6H_6	 (—)	926
	Piperidine	Boiling $i\text{-C}_3\text{H}_7\text{OH}$	 (75)	909
	"	Room	 (—)	739
	$\text{CH}_3\text{CO}_2\text{NH}_4$	Boiling C_6H_6	 (—)	662

Note: References 285 to 1153 are on pp. 582-599.

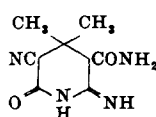
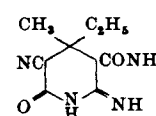
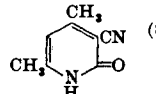
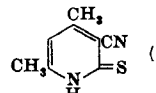
^b Ethyl cyanoacetate was used in this reaction.

^{aa} *t*-Butyl cyanoacetate was also used.

TABLE VIII
CONDENSATIONS WITH CYANOACETAMIDES AND THIOCYANOACETAMIDES

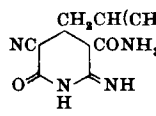
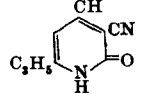
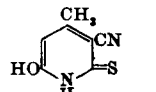
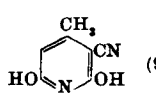
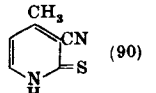
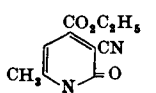



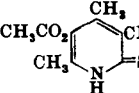
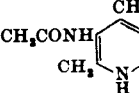
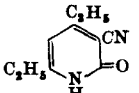
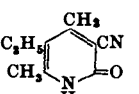
The R group in the amide is specified only where its identity is not clear from the structure of the product(s). The use of a thioacetamide is shown by the presence of sulfur in the product(s).

A. Acyclic Aldehydes or Ketones				
Aldehyde or Ketone	Catalyst	Temperature	Product(s) and Yield(s) (%)	Refs.
Acetone	Piperidine	Room	 (93)	927
$(\text{CH}_3)_2\text{CHCHO}$	$(\text{C}_2\text{H}_5)_2\text{NH}$ or piperidine	"	$i\text{-C}_3\text{H}_7\text{CH}[\text{CH}(\text{CN})\text{CONH}_2]_2$ (79)	159, 928
$\text{CH}_3\text{COC}_2\text{H}_5$	Piperidine	"	 (90)	927
Acetylacetone	Piperidine or $(\text{C}_2\text{H}_5)_2\text{NH}/\text{C}_2\text{H}_5\text{OH}$	80°	 (87)	161, 162
	$(\text{C}_2\text{H}_5)_2\text{NCH}_2\text{CH}_2\text{OH}$	Boiling $\text{C}_2\text{H}_5\text{OH}$	 (100)	929

Note: References 285 to 1153 are on pp. 582-599.


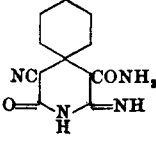

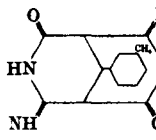
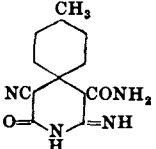
TABLE VIII—Continued
CONDENSATIONS WITH CYANOACETAMIDES AND THIOCYANOACETAMIDES

A. Acyclic Aldehydes or Ketones—Continued				
Aldehyde or Ketone	Catalyst	Temperature	Product(s) and Yield(s) (%)	Refs.
3-Methylbutanal	$(\text{C}_2\text{H}_5)_2\text{NH}/\text{aq. alcohol}$	Room	 (30)	159
Hexane-2,4-dione	$(\text{C}_2\text{H}_5)_2\text{NH}/\text{C}_2\text{H}_5\text{OH}$	"	 (—)	162
$\text{CH}_3\text{COCH}_2\text{CO}_2\text{C}_2\text{H}_5$	$(\text{C}_2\text{H}_5)_2\text{NCH}_2\text{CH}_2\text{OH}$	Boiling $\text{C}_2\text{H}_5\text{OH}$	 (42)	929
	Piperidine	Boiling CH_3OH	 (94)	729
$\text{CH}_3\text{COCH}_2\text{CH}(\text{OCH}_3)_2$	$(\text{C}_2\text{H}_5)_2\text{NCH}_2\text{CH}_2\text{OH}$	Boiling $\text{CH}_3\text{CO}_2\text{H}$	 (90)	929
Ethyl acetylpyruvate	NH_3 or $(\text{C}_2\text{H}_5)_2\text{NH}/\text{alcohol}$	40-50°, then cooled (or 0°)	 (Quant.)	162

	$(C_2H_5)_3NCH_2CH_2OH$	Boiling C_2H_5OH	 (93)	929
3-Acetoxy-pentane-2,4-dione	"	"	 (88)	929
3-Acetamidopentane-2,4-dione	"	"	 (60)	929
Heptane-3,5-dione	$(C_2H_5)_3NH$	50°	 (90)	99
3-Ethylpentane-2,4-dione	$(C_2H_5)_3NH$ /alcohol	Room	 (—)	162
Ethyl levulinate	$CH_3CO_2NH_4$	Boiling C_2H_5	$CH_3CCH_2CH_2CO_2C_2H_5$ \parallel $C(CN)CONH_2$ (20)	135
Heptanal	Piperidine/aq. C_2H_5OH	Room	$n-C_6H_{13}CH[CH(CN)CONH_2]_2$ (87)	159

Note: References 285 to 1153 are on pp. 582-599

TABLE VIII—Continued
CONDENSATIONS WITH CYANOACETAMIDES AND THIOCYANOACETAMIDES

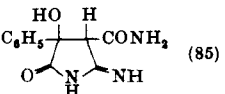
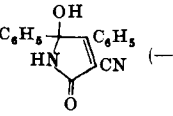
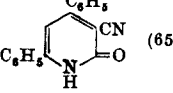
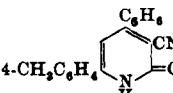
B. Alicyclic Ketones				
Aldehyde or Ketone	Catalyst	Temperature	Product(s) and Yield(s) (%)	Refs.
Cyclopentanone	Piperidine	Room	 $C(CN)CONH_2$ (Low)	813
Methyl cyclopropyl ketone	$CH_3CO_2NH_4$	Boiling C_2H_5	$C_2H_5C(CH_3)=C(CN)CONH_2$ (73)	158
Cyclohexanone	Piperidine	Room	 (92)	927
	Dowex 3 acetate	Boiling C_2H_5	$C(CN)CONH_2$  (63)	141
3-Methylcyclohexanone	Piperidine	25°	 (67)	160
4-Methylcyclohexanone	"	25°	 (72)	160

C. Aralkyl Aldehydes or Ketones				
3-Bromo-5-fluoro-2-hydroxyacetophenone	CH ₃ CO ₂ NH ₄	Boiling C ₆ H ₆	3-Br-5-F-2-HOC ₆ H ₃ C(CH ₃)=C(CN)CON(CH ₃) ₂ (—)	854
3-Bromo-4-hydroxyacetophenone	"	"	3-Br-4-HOC ₆ H ₃ C(CH ₃)=C(CN)CON(CH ₃) ₂ (—)	854
2-Hydroxyacetophenone	"	"	2-HOC ₆ H ₄ C(CH ₃)=C(CN)CON(CH ₃) ₂ (—)	854
4-Hydroxyacetophenone	"	"	4-HOC ₆ H ₄ C(CH ₃)=C(CN)CONH ₂ (—)	854
2-Bromo-4-methoxyacetophenone	"	"	2-Br-4-CH ₃ OC ₆ H ₃ C(CH ₃)=C(CN)CON(CH ₃) ₂ (—)	854
4-Methoxyacetophenone	"	"	4-CH ₃ OC ₆ H ₄ C(CH ₃)=C(CN)CON(CH ₃) ₂ (—)	854
1-(5'-Chloro-2'-hydroxyphenyl)but-2-en-1-one	"	"	5-Cl-2-HOC ₆ H ₃ CCH=CHC(=O)C(CN)CON(CH ₃) ₂ (—)	854
Benzoylacetone	(C ₂ H ₅) ₂ NH	Boiling C ₆ H ₅ OH	$\text{C}_6\text{H}_5\text{CH}=\text{CHC}(\text{CN})=\text{O} + \text{C}_6\text{H}_5\text{CH}=\text{CHC}(\text{CN})=\text{O}$ (Major) (Minor)	162
	(C ₂ H ₅) ₂ NCH ₂ CH ₂ OH	"	$\text{C}_6\text{H}_5\text{CH}=\text{CHC}(\text{CN})=\text{S}$ (95)	929
4-Hydroxy-2,3-dimethylacetophenone	CH ₃ CO ₂ NH ₄	Boiling C ₆ H ₆	4-HO-2,3-(CH ₃) ₂ -C ₆ H ₃ C(CH ₃)=C(CN)CON(CH ₃) ₂ (—)	854
5-Bromo-2-allyloxyacetophenone	"	"	5-Br-2-C ₃ H ₅ OC ₆ H ₃ C(CH ₃)=C(CN)CON(CH ₃) ₂ (—)	854
1-Phenylpentane-1,3-dione	(C ₂ H ₅) ₂ NH	Boiling C ₆ H ₅ OH	$\text{C}_6\text{H}_5\text{CH}=\text{CHC}(\text{CN})=\text{O}$ (—)	162
2-Hydroxy-3-allylacetophenone	CH ₃ CO ₂ NH ₄	Boiling C ₆ H ₆	2-HO-3-C ₃ H ₅ C ₆ H ₃ C(CH ₃)=C(CN)CON(CH ₃) ₂ (—)	854
4-Hydroxy-3-allylacetophenone	"	"	4-HO-3-C ₃ H ₅ C ₆ H ₃ C(CH ₃)=C(CN)CON(CH ₃) ₂ (—)	854

Note: References 285 to 1153 are on pp. 582-599.

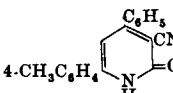
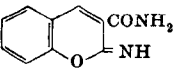
TABLE VIII—Continued
CONDENSATIONS WITH CYANOACETAMIDES AND THIOCYANOACETAMIDES

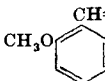
C. Aralkyl Aldehydes or Ketones—Continued				
Aldehyde or Ketone	Catalyst	Temperature	Product(s) and Yield(s) (%)	Refs.
4-Dimethylamino-cinnamaldehyde	Piperidinium acetate	Boiling C ₂ H ₅ OH	4-(CH ₃) ₂ NC ₆ H ₄ CH=CHCH=C(CN)CONH ₂ (—)	760
	"	"	4-(CH ₃) ₂ NC ₆ H ₄ CH=CH-CH=C(CN)CONHC ₆ H ₅ (—)	760
3-Bromo-4-methoxybutyrophenone	CH ₃ CO ₂ NH ₄	Boiling C ₆ H ₆	3-Br-4-CH ₃ OC ₆ H ₃ C(C ₃ H ₇ , n)=C(CN)CONH ₂ (—)	854
2-Hydroxy-3-allyl-5-methylacetophenone	"	"	2-HO-3-C ₃ H ₅ -5-CH ₃ C ₆ H ₃ -C(CH ₃)=C(CN)CON(CH ₃) ₂ (—)	854
1-(2'-Methoxyphenyl)pent-4-en-1-one	"	"	$\text{C}(\text{CN})\text{CONH}_2$ (—)	854
	"	"	$2\text{-CH}_3\text{OC}_6\text{H}_4\text{CCH}_2\text{CH}_2\text{CH}=\text{CH}_2$ (—)	854
3-Chloro-4-ethoxybutyrophenone	"	"	3-Cl-4-C ₂ H ₅ OC ₆ H ₃ C(C ₃ H ₇ , n)=C(CN)CONH ₂ (—)	854
2-Hydroxy-5-ethylbutyrophenone	"	"	2-HO-5-C ₂ H ₅ C ₆ H ₃ C(C ₃ H ₇ , n)=C(CN)CONH ₂ (—)	854
2-Allyloxybutyrophenone	"	"	2-C ₃ H ₅ OC ₆ H ₄ C(C ₃ H ₇ , n)=C(CN)CONH ₂ (—)	854
1-(4'-Methoxyphenyl)-3-methylpent-2-en-1-one	"	"	$4\text{-CH}_3\text{OC}_6\text{H}_4\text{CCH}=\text{C}(\text{CH}_3)\text{C}_2\text{H}_5$ $\text{C}(\text{CN})\text{CONH}_2$ (—)	854
1-(2'-Hydroxy-4',5'-dimethylphenyl)pent-2-en-1-one	"	"	$2\text{-HO-4,5-(CH}_3)_2\text{C}_6\text{H}_3\text{C}-\text{CH}=\text{CHC}_2\text{H}_5$ $\text{C}(\text{CN})\text{CONH}_2$ (—)	854
	"	"	$2\text{-HO-4,5-(CH}_3)_2\text{C}_6\text{H}_3\text{C}-\text{CCH}=\text{CHC}_2\text{H}_5$ $\text{C}(\text{CN})\text{CON}(\text{CH}_3)_2$ (—)	854
4-Ethoxy-3-methylbutyrophenone	"	"	4-C ₂ H ₅ O-3-CH ₃ C ₆ H ₃ C(C ₃ H ₇ , n)=C(CN)CONH ₂ (—)	854

2-Hydroxy-6-methyl-4-ethylbutyrophenone	"	"	$2\text{-HO-6-CH}_3\text{-4-C}_2\text{H}_5\text{C}_6\text{H}_4\text{C(C}_2\text{H}_5\text{)}_2\text{=C(CN)CONH}_2\text{ (—)}$	854
Phenylglyoxylic acid anilide	$(\text{C}_2\text{H}_5)_2\text{NH/aq. C}_2\text{H}_5\text{OH}$	Room		163
Benzil	$(\text{C}_2\text{H}_5)_2\text{NH}$	$\text{C}_2\text{H}_5\text{OH, hot}$		763
1-(2'-Methoxyphenyl)hept-6-en-1-one	$\text{CH}_3\text{CO}_2\text{NH}_4$	Boiling C_6H_6	$2\text{-CH}_3\text{OC}_6\text{H}_4\text{C(CH}_3)_2\text{CH=CH}_2\text{C(CN)CONH}_2\text{ (—)}$	854
"	"	"	$2\text{-CH}_3\text{OC}_6\text{H}_4\text{C(CH}_3)_2\text{CH=CH}_2\text{C(CN)CON(CH}_3)_2\text{ (—)}$	854
4-Propoxy-2-methylbutyrophenone	"	"	$4\text{-C}_3\text{H}_7\text{O-2-CH}_3\text{C}_6\text{H}_4\text{C(C}_3\text{H}_7\text{)}_2\text{=C(CN)CONH}_2\text{ (—)}$	854
Dibenzoylmethane	$(\text{C}_2\text{H}_5)_2\text{NH}$	Room (32°)		99
4-Benzoyloxyacetophenone	$\text{CH}_3\text{CO}_2\text{NH}_4$	Boiling C_6H_6	$4\text{-C}_6\text{H}_5\text{CH}_2\text{OC}_6\text{H}_4\text{C(CH}_3)_2\text{=C(CN)CONH}_2\text{ (—)}$	854
4-Butoxy-2-methylbutyrophenone	"	"	$4\text{-C}_4\text{H}_9\text{CH}_2\text{OC}_6\text{H}_4\text{C(CH}_3)_2\text{=C(CN)CON(CH}_3)_2\text{ (—)}$	854
4-Propoxy-2,5-dimethylbutyrophenone	"	"	$4\text{-C}_4\text{H}_9\text{O-2-CH}_3\text{C}_6\text{H}_4\text{C(C}_3\text{H}_7\text{)}_2\text{=C(CN)CONH}_2\text{ (—)}$	854
"	"	"	$4\text{-C}_3\text{H}_7\text{O-2,5-(CH}_3)_2\text{C}_6\text{H}_4\text{C(C}_3\text{H}_7\text{)}_2\text{=C(CN)CONH}_2\text{ (—)}$	854
Benzoyl-4-methylbenzoylmethane	$(\text{C}_2\text{H}_5)_2\text{NH}$	Room (32°)		99

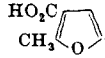
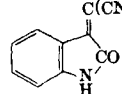
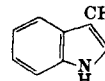
Note: References 285 to 1153 are on pp. 582-599.

TABLE VIII—Continued
CONDENSATIONS WITH CYANOACETAMIDES AND THIOCYANOACETAMIDES

C. Aromatic Aldehydes or Ketones—Continued				
Aldehyde or Ketone	Catalyst	Temperature	Product(s) and Yield(s) (%)	Refs.
1-(2'-Methoxyphenyl)-non-2-en-1-one	$\text{CH}_3\text{CO}_2\text{NH}_4$	Boiling C_6H_6	$2\text{-CH}_3\text{OC}_6\text{H}_4\text{CCH=CHC}_6\text{H}_4\text{C(CN)CONH}_2\text{ (—)}$	854
"	"	"	$2\text{-CH}_3\text{OC}_6\text{H}_4\text{CCH=CHC}_6\text{H}_4\text{C(CN)CON(CH}_3)_2\text{ (—)}$	854
2-Isopentyloxy-5-methylbutyrophenone	"	"	$2\text{-i-C}_5\text{H}_{11}\text{O-5-CH}_3\text{C}_6\text{H}_4\text{C(C}_3\text{H}_7\text{)}_2\text{=C(CN)CONH}_2\text{ (—)}$	854
$\text{C}_6\text{H}_5\text{C(OCH}_3)_2\text{=CHCOC}_6\text{H}_4\text{CH}_3\text{-4}$	$(\text{C}_2\text{H}_5)_2\text{NH}$	Room (32°)		99
4-Methoxy-3-phenylbutyrophenone	$\text{CH}_3\text{CO}_2\text{NH}_4$	Boiling C_6H_6	$4\text{-CH}_3\text{O-3-C}_6\text{H}_5\text{C}_6\text{H}_4\text{C(C}_3\text{H}_7\text{)}_2\text{=C(CN)CONH}_2\text{ (—)}$	854
4-Dodecyloxyacetophenone	"	"	$4\text{-C}_{12}\text{H}_{25}\text{OC}_6\text{H}_4\text{C(CH}_3)_2\text{=C(CN)CONH}_2\text{ (—)}$	854
"	"	"	$4\text{-C}_{12}\text{H}_{25}\text{OC}_6\text{H}_4\text{C(CH}_3)_2\text{=C(CN)CON(CH}_3)_2\text{ (—)}$	854
D. Aromatic Aldehydes or Ketones				
2-Nitrobenzaldehyde	$(\text{C}_2\text{H}_5)_2\text{NH/C}_2\text{H}_5\text{OH}$	Below 35°	$2\text{-O}_2\text{NC}_6\text{H}_4\text{CH=C(CN)CONH}_2\text{ (Quant.)}$	767
Benzaldehyde	Piperidine	Water bath	$\text{C}_6\text{H}_5\text{N(CH}_3)_2\text{COC(CN)=CHC}_6\text{H}_5\text{* (93)}$	931
"	"	0°	$\text{C}_6\text{H}_5\text{CH[CH(CN)CON(CH}_3)_2\text{C}_6\text{H}_5\text{]}_2\text{* (33)}$	931
Salicylaldehyde	Piperidine/aq. CH_3OH	Room		111

4-Methoxybenzaldehyde (anisaldehyde)	„	„	$4\text{-CH}_3\text{OC}_6\text{H}_4\text{CH}=\text{C}(\text{CN})\text{CONH}_2$ (75)	111
3-Methoxy-4-hydroxybenzaldehyde (vanillin)	„	„	$3\text{-CH}_3\text{O-4-HOC}_6\text{H}_3\text{CH}=\text{C}(\text{CN})\text{CONH}_2$ (80)	111
4-Methoxyisophthalaldehyde	Piperidine + pyridine	Water bath	 (—)	491
4-(CH ₃) ₂ NC ₆ H ₄ CHO	Piperidinium acetate	Boiling C ₂ H ₅ OH	$4\text{-(CH}_3)_2\text{NC}_6\text{H}_4\text{CH}=\text{C}(\text{CN})\text{CONH}_2$ (79)	762, 894
1-Naphthaldehyde	Morpholine	Steam bath	$1\text{-C}_{10}\text{H}_7\text{CH}=\text{C}(\text{CN})\text{CONH}_2$ (74)	899
4-Di-(2'-chloroethyl)aminobenzaldehyde	Piperidine/dioxane	Room	$4\text{-(ClCH}_2\text{CH}_2)_2\text{NC}_6\text{H}_4\text{CH}=\text{C}(\text{CN})\text{CONH}_2$ (68)	278
Benzophenone imine	None	115°	$(\text{C}_6\text{H}_5)_2\text{C}=\text{C}(\text{CN})\text{CONH}_2$ (100)	164

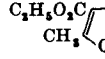
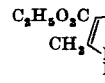
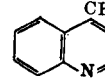
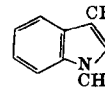
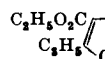
E. Heterocyclic Aldehydes or Ketones

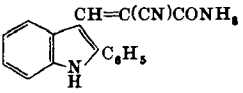
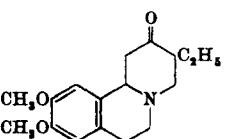
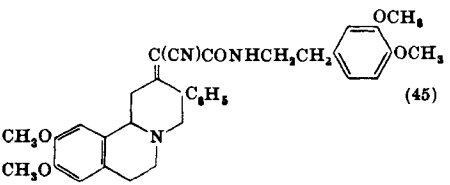
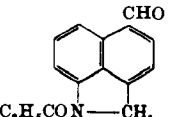
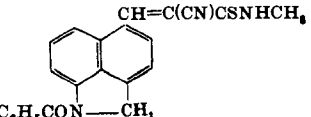
2-Methyl-5-formyl-furan-3-carboxylic acid	(C ₂ H ₅) ₂ NH/C ₂ H ₅ OH	Room	 (71)	777
Isatin	(C ₂ H ₅) ₂ NH	Boiling C ₂ H ₅ OH	 (—)	932
Indole-3-carboxaldehyde	Piperidine	100°	 (90)	237

Note: References 285 to 1153 are on pp. 582-599.

* The disubstituted acetamide derivative, CNCH₂CON(CH₃)C₆H₅, was used in this reaction.

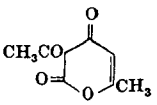
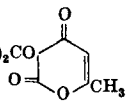
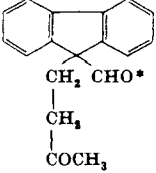
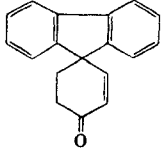
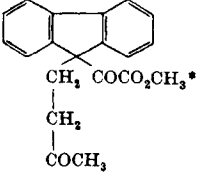
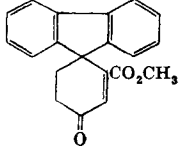
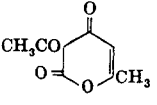
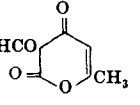
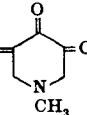
TABLE VIII—Continued
CONDENSATIONS WITH CYANOACETAMIDES AND THIOCYANOACETAMIDES

E. Heterocyclic Aldehydes or Ketones—Continued				
Aldehyde or Ketone	Catalyst	Temperature	Product(s) and Yield(s) (%)	Refs.
Ethyl 2-methyl-5-formylfuran-3-carboxylate	(C ₂ H ₅) ₂ NH/C ₂ H ₅ OH	Room	$\text{C}_2\text{H}_5\text{O}_2\text{C-CH}_2\text{-}$  (62)	777
Ethyl 2-methyl-5-formylpyrrole-3-carboxylate	„	Less than 10°	$\text{C}_2\text{H}_5\text{O}_2\text{C-CH}_2\text{-}$  (86)	780
Quinoline-4-carboxaldehyde hydrate	(C ₂ H ₅) ₂ NH	Boiling C ₂ H ₅ OH	 (90)	42
1-Methylindole-3-carboxaldehyde	Piperidine	100°	 (—)	237
Ethyl 2-ethyl-5-formylfuran-3-carboxylate	(C ₂ H ₅) ₂ NH	Room	No reaction	777
Ethyl 3-carbethoxy-5-formyl-2-furylacetate	„	„	No reaction	777
Ethyl 2-phenyl-5-formylfuran-3-carboxylate	Diethylamine/C ₂ H ₅ OH	„	$\text{C}_2\text{H}_5\text{O}_2\text{C-CH}_2\text{-}$  (73)	777

2-Phenylindole-3-carboxaldehyde	Piperidine	Boiling C_2H_5OH		(84)	923
	$CH_3CO_2NH_4$	Boiling C_6H_6		(45)	114
	"	"		(—)	662

Note: References 285 to 1153 are on pp. 582-599.

TABLE IX
CONDENSATIONS WITH KETONES

A. Acyclic Aldehydes					
Aldehyde or Ketone	Ketone	Catalyst	Temperature	Product(s) and Yield(s) (%)	Refs.
Formaldehyde	Desoxybenzoin	Piperidinium acetate	Boiling CH ₃ OH	CH ₂ =C(C ₆ H ₅)COC ₆ H ₅ (67)	933
	4-Methyldeoxybenzoin	"	"	CH ₂ =C(C ₆ H ₅)COC ₆ H ₄ CH ₃ -4 (53)	933
	4-Methoxydesoxybenzoin	"	"	CH ₂ =C(C ₆ H ₅)COC ₆ H ₄ OCH ₃ -4 (81)	933
	4,4'-Dimethoxydesoxybenzoin	"	"	CH ₂ =C(C ₆ H ₄ OCH ₃ -4)COC ₆ H ₄ OCH ₃ -4 (69)	933
	4-Chlorodesoxybenzoin	"	"	CH ₂ =C(C ₆ H ₅)COC ₆ H ₄ Cl-4 (67)	933
	4'-Methoxydesoxybenzoin	"	"	CH ₂ =C(C ₆ H ₄ OCH ₃ -4)COC ₆ H ₅ (54)	933
	4'-Nitrodesoxybenzoin	"	"	CH ₂ =C(C ₆ H ₄ NO ₂ -4)COC ₆ H ₅ (46)	933
n-Butyraldehyde	Pyruvic acid	(C ₂ H ₅)NH	Room	n-C ₃ H ₇ CH=CHCOCOC ₆ H ₅ (5)	934
2,4,6-Octatrienal	Biacetyl	Piperidine C ₆ H ₅ OH	"	CH ₃ (CH=CH) ₄ COCO(CH=CH) ₄ CH ₃ (Small) CH ₃ (CH=CH) ₄ COCOCH ₃	935
B. Aromatic Aldehydes					
Cinnamaldehyde	Biacetyl	Piperidine or piperidinium acetate	Boiling C ₆ H ₅ OH	C ₆ H ₅ (CH=CH) ₂ COCO(CH=CH) ₂ C ₆ H ₅ (57)	936, 937, 938
		Piperidine	Boiling CHCl ₃	C ₆ H ₅ (CH=CH) ₂ CO  (57)	939
5-Phenylpentadienal	Biacetyl	Piperidine or piperidinium acetate	Boiling C ₂ H ₅ OH	C ₆ H ₅ (CH=CH) ₃ COCO(CH=CH) ₃ C ₆ H ₅ (32)	936, 937, 938
7-Phenylheptatrienal	Biacetyl	"	Boiling CH ₃ OH	C ₆ H ₅ (CH=CH) ₄ COCO(CH=CH) ₄ C ₆ H ₅ (5)	936, 938
9-Phenylnonatetraenal	Biacetyl	Piperidinium acetate	"	C ₆ H ₅ (CH=CH) ₆ COCO(CH=CH) ₆ C ₆ H ₅ (-)	938
		"	Boiling CH ₃ CO ₂ H	 (73)	940
		"	"	 (77)	940
C. Aromatic Aldehydes or Benzoylformanilide					
3,4-Dichlorobenzaldehyde		Piperidine	Boiling CHCl ₃	3,4-Cl ₂ C ₆ H ₃ CH=CHCO  (46)	939
4-Bromobenzaldehyde	Biacetyl	Piperidinium acetate	—	4-BrC ₆ H ₄ CH=CHCOCOCH=CHC ₆ H ₄ Br-4 (-)	941
2-Chlorobenzaldehyde	N-Methyl-4-piperidone	Piperidine	Boiling C ₂ H ₅ OH	2-ClC ₆ H ₄ CH  =CHC ₆ H ₄ Cl-2 (80)	167

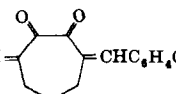
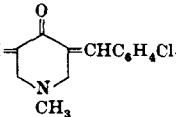
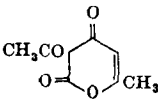
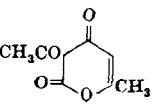
Note: References 285 to 1153 are on pp. 582-599.

* The condensation was intramolecular.

TABLE IX—Continued
CONDENSATIONS WITH KETONES

440

ORGANIC REACTIONS

C. Aromatic Aldehydes or Benzoylformanilide—Continued					
Aldehyde or Ketone	Ketone	Catalyst	Temperature	Product(s) and Yield(s) (%)	Refs.
2-Chlorobenzaldehyde (<i>contd.</i>)	Cycloheptane-1,2-dione	Piperidine	Boiling C_2H_5OH	 2- $ClC_6H_4CH=$ (15)	166
4-Chlorobenzaldehyde	Biacetyl	Piperidinium acetate	—	4- $ClC_6H_4CH=CHCOCOCH=CHC_6H_4Cl$ -4 (—)	941
	N-Methyl-4-piperidone	Piperidine	Boiling C_2H_5OH	 4- $ClC_6H_4CH=$ (89)	167
2-Nitrobenzaldehyde		"	Boiling $CHCl_3$	2- $O_2NC_6H_4CH=CHCO$ (65)	939
3-Nitrobenzaldehyde	N-Methyl-4-piperidone	"	Boiling C_2H_5OH	3- $O_2NC_6H_4CH=CHC_6H_4NO_2$ -3 (82)	167
		"	Boiling $CHCl_3$	3- $O_2NC_6H_4CH=CHCO$ (60)	939
4-Nitrobenzaldehyde	Cycloheptane-1,2-dione	"	Boiling C_2H_5OH	4- $O_2NC_6H_4CH=$ (29)	166
	N-Methyl-4-piperidone	"	"	4- $O_2NC_6H_4CH=CHC_6H_4NO_2$ -4 (100)	167
	Tetrahydro- γ -pyrone	Piperidinium acetate	"	4- $O_2NC_6H_4CH=CHC_6H_4NO_2$ -4 (60)	942
	Tetrahydrothiopyran-4-one	"	"	4- $O_2NC_6H_4CH=CHC_6H_4NO_2$ -4 (77)	942
Benzaldehyde	Biacetyl	"	"	$C_6H_5CH=CHCOCOCH=CHC_6H_5$ (10)	937
	Methyl benzyl ketone	Piperidine (+ $n-C_6H_{11}CO_2H$)	Boiling C_6H_6	$C_6H_5CH=C(COCH_3)C_6H_5$ (74)	168, 69, 943
	Desoxybenzoin	"	"	$C_6H_5CH=C(COC_6H_5)C_6H_5$ (60)	69, 168
	Dibenzyl ketone	Piperidine	Boiling C_2H_5OH	$C_6H_5CH=C(C_6H_5)COCH_2C_6H_5$ (—)	22
	"	Piperidine/ C_2H_5OH	Room	$C_6H_5CH(NC_6H_{10})CH(C_6H_5)COCH_2C_6H_5$ † (75)	22

Note: References 285 to 1153 are on pp. 582–599.

† This product was obtained in better yield using benzaldehyde dipiperide.

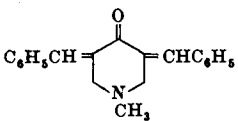
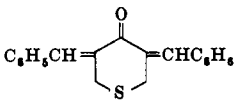
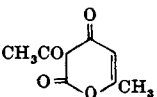
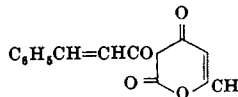
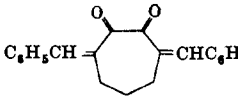
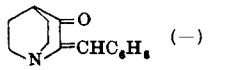
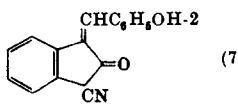
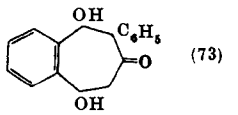
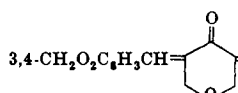
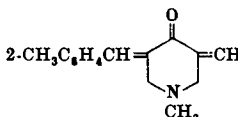
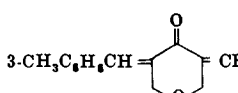
THE KNOEVENAGEL CONDENSATION

441

TABLE IX—Continued
CONDENSATIONS WITH KETONES

442

ORGANIC REACTIONS

C. Aromatic Aldehydes or Benzoylformanilide—Continued					
Aldehyde or Ketone	Ketone	Catalyst	Temperature	Product(s) and Yield(s) (%)	Refs.
Benzaldehyde (contd.)	N-Methyl-4-piperidone	Piperidine	Boiling C ₆ H ₅ OH	 (57)	167
	Tetrahydrothiopyran-4-one	Piperidinium acetate	"	 (76)	942
		Piperidine	Boiling CHCl ₃	 (55)	939
	Cycloheptane-1,2-dione	"	Boiling C ₆ H ₅ OH	 (34)	165
	Quinuelidone	"	"	 (—)	944
Benzaldehyde anil	Dibenzyl ketone	—	Room	C ₆ H ₅ CH(NHC ₆ H ₅)CH(C ₆ H ₅)COCH ₂ C ₆ H ₅ (85)	24
Salicylaldehyde	1-Cyanoindan-2-one	Piperidine/CH ₃ OH	"	 (70)	945
Phthalaldehyde	Methyl benzyl ketone	(C ₆ H ₅) ₂ NH	50°, then room	 (73)	176
3,4-Methylenedioxybenzaldehyde (piperonal)	Biacetyl	Piperidinium acetate	—	3,4-CH ₂ O ₂ C ₆ H ₃ CH=CHCOCOCH=	941
	Dibenzyl ketone	C ₆ H ₅ NH	Room	CHC ₆ H ₅ O ₂ CH ₂ -3,4 (—)	24
	"	Piperidine/C ₆ H ₅ OH	"	3,4-CH ₂ O ₂ C ₆ H ₃ CH[N(C ₂ H ₅) ₂]CH(C ₆ H ₅)COCH ₂ C ₆ H ₅ (70)	22
	"	"	"	3,4-CH ₂ O ₂ C ₆ H ₃ CH(NC ₂ H ₅)CH(C ₆ H ₅)COCH ₂ C ₆ H ₅ (—)	22
Piperonal anil	Tetrahydro-γ-pyrone	Piperidinium acetate	Boiling C ₃ H ₅ OH	 (55)	942
	Dibenzyl ketone	—	Room	3,4-CH ₂ O ₂ C ₆ H ₃ CH(NHC ₆ H ₅)CH(C ₆ H ₅)COCH ₂ C ₆ H ₅ (92)	24
2-Methylbenzaldehyde	N-Methyl-4-piperidone	Piperidine	Boiling C ₆ H ₅ OH	 (69)	167
3-Methylbenzaldehyde	Tetrahydro-γ-pyrone	Piperidinium acetate	"	 (33)	942

Note: References 285 to 1153 are on pp. 582-599.

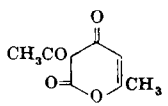
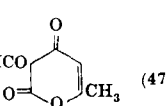
THE KNOEVENAGEL CONDENSATION

443

TABLE IX—Continued
CONDENSATIONS WITH KETONES

444

ORGANIC REACTIONS

C. Aromatic Aldehydes or Benzoylformanilide—Continued					
Aldehyde or Ketone	Ketone	Catalyst	Temperature	Product(s) and Yield(s) (%)	Refs.
4-Methylbenzaldehyde	N-Methyl-4-piperidone	Piperidine	Boiling C ₂ H ₅ OH	4-CH ₃ C ₆ H ₄ CH=CHC(=O)N(CH ₃)C ₆ H ₄ CH ₃ -4 (63)	167
	Tetrahydrothiopyran-4-one	Piperidinium acetate	„	4-CH ₃ C ₆ H ₄ CH=CHC(=O)SC ₆ H ₄ CH ₃ -4 (75)	942
	Cycloheptane-1,2-dione	Piperidine	„	4-CH ₃ C ₆ H ₄ CH=CHC(=O)C ₆ H ₄ CH ₃ -4 (18)	166
2-Methoxybenzaldehyde	Biacetyl	Piperidinium acetate	—	2-CH ₃ OC ₆ H ₄ CH=CHCOC(=O)CH=CHC ₆ H ₄ OCH ₃ -2 (—)	941
4-Methoxybenzaldehyde (anisaldehyde)	Biacetyl	„	—	4-CH ₃ OC ₆ H ₄ CH=CHCOC(=O)CH=CHC ₆ H ₄ OCH ₃ -4 (—)	941
	Dibenzyl ketone	(C ₂ H ₅) ₂ NH	Room	4-CH ₃ OC ₆ H ₄ CH[N(C ₂ H ₅) ₂]CH(C ₆ H ₅)COCH ₂ C ₆ H ₅ † (60)	24
	Cycloheptane-1,2-dione	Piperidine	Boiling C ₂ H ₅ OH	4-CH ₃ OC ₆ H ₄ CH=CHC(=O)C ₆ H ₄ OCH ₃ -4 (14)	166
	Tetrahydrothiopyran-4-one	Piperidinium acetate	„	4-CH ₃ OC ₆ H ₄ CH=CHC(=O)SC ₆ H ₄ OCH ₃ -4 (92)	942
	N-Methyl-4-piperidone	Piperidine	„	4-CH ₃ OC ₆ H ₄ CH=CHC(=O)N(CH ₃)C ₆ H ₄ OCH ₃ -4 (66)	167
Anisaldehyde anil	Dibenzyl ketone	—	Room	4-CH ₃ OC ₆ H ₄ CH(NHC ₆ H ₅)CH(C ₆ H ₅)COCH ₂ C ₆ H ₅ (86)	24
2-Nitro-3,4-dimethoxybenzaldehyde	Acetophenone	Piperidine	Water bath	2-O ₂ N-3,4-(CH ₃ O) ₂ C ₆ H ₂ CH=CHCOC(=O)CH ₃ (—)	187
	4-Bromoacetophenone	„	„	2-O ₂ N-3,4-(CH ₃ O) ₂ C ₆ H ₂ CH=CHCOC(=O)CH ₂ Br-4 (—)	187
2-Ethoxybenzaldehyde	Biacetyl	Piperidinium acetate	—	2-C ₂ H ₅ OC ₆ H ₄ CH=CHCOC(=O)CH=CHC ₆ H ₄ OC ₂ H ₅ -2 (—)	941
4-Ethoxybenzaldehyde	Tetrahydro-γ-pyrone	„	Boiling C ₂ H ₅ OH	4-C ₂ H ₅ OC ₆ H ₄ CH=CHC(=O)C ₆ H ₄ OC ₂ H ₅ -4 (56)	942
2,3-Dimethoxybenzaldehyde		Piperidine	Boiling CHCl ₃	2,3-(CH ₃ O) ₂ C ₆ H ₃ CH=CHCO-  (47)	939
	Tetrahydro-γ-pyrone	Piperidinium acetate	Boiling C ₂ H ₅ OH	2,3-(CH ₃ O) ₂ C ₆ H ₃ CH=CHC(=O)C ₆ H ₃ (OCH ₃) ₂ -2,3 (50)	942

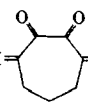
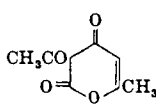
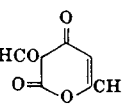
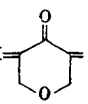
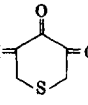
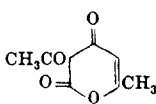
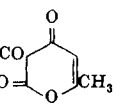
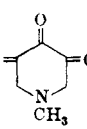
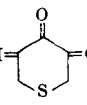
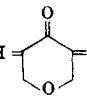
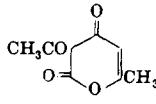
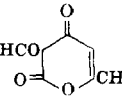
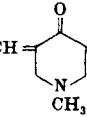
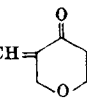
Note: References 285 to 1153 are on pp. 582–599.

† A similar compound was obtained using piperidine.²⁴

THE KNOEVENAGEL CONDENSATION

445

TABLE IX—Continued
CONDENSATIONS WITH KETONES

C. Aromatic Aldehydes or Benzoylformanilide—Continued					
Aldehyde or Ketone	Ketone	Catalyst	Temperature	Product(s) and Yield(s) (%)	Refs.
3,4-Dimethoxybenzaldehyde (veratraldehyde)	Cycloheptane-1,2-dione	Piperidine	Boiling C ₂ H ₅ OH	3,4-(CH ₃ O) ₂ C ₆ H ₃ CH=CHC ₆ H ₃ (OCH ₃) ₂ -3,4 	166 (8)
		"	Boiling CHCl ₃	3,4-(CH ₃ O) ₂ C ₆ H ₃ CH=CHCO- 	939 (46)
	Tetrahydro-γ-pyrone	Piperidinium acetate	Boiling C ₂ H ₅ OH	3,4-(CH ₃ O) ₂ C ₆ H ₃ CH=CHC ₆ H ₃ (OCH ₃) ₂ -3,4 	942 (58)
4-Dimethylamino- benzaldehyde	Tetrahydrothio- pyran-4-one	"	"	3,4-(CH ₃ O) ₂ C ₆ H ₃ CH=CHC ₆ H ₃ (OCH ₃) ₂ -3,4 	942 (67)
	Dibenzyl ketone	Piperidine C ₂ H ₅ OH	Room	4-(CH ₃) ₂ NC ₆ H ₄ CH(NC ₅ H ₁₀)CH(C ₆ H ₅)COCH ₂ C ₆ H ₅ (—)	22
		Piperidine	Boiling CHCl ₃	4-(CH ₃) ₂ NC ₆ H ₄ CH=CHCO- 	939 (63)
N-Methyl-4- piperidone	N-Methyl-4- piperidone	Piperidine	Boiling C ₂ H ₅ OH	4-(CH ₃) ₂ NC ₆ H ₄ CH=CHC ₆ H ₄ N(CH ₃) ₂ -4 	167 (58)
	Tetrahydrothio- pyran-4-one	Piperidinium acetate	"	4-(CH ₃) ₂ NC ₆ H ₄ CH=CHC ₆ H ₄ N(CH ₃) ₂ -4 	942 (77)
	Tetrahydro-γ- pyrone	"	"	4-(CH ₃) ₂ NC ₆ H ₄ CH=CHC ₆ H ₄ N(CH ₃) ₂ -4 	942 (42)
4-Isopropylbenz- aldehyde		Piperidine	Boiling CHCl ₃	4-(CH ₃) ₂ CHC ₆ H ₄ CH=CHCO- 	939 (65)
	N-Methyl-4- piperidone	"	Boiling C ₂ H ₅ OH	4-(CH ₃) ₂ CHC ₆ H ₄ CH=CHC ₆ H ₄ N(CH ₃) ₂ -4 	167 (36)
	Tetrahydro-γ- pyrone	Piperidinium acetate	"	4-(CH ₃) ₂ CHC ₆ H ₄ CH=CHC ₆ H ₄ N(CH ₃) ₂ -4 	942 (50)

Note: References 285 to 1153 are on pp. 582-599.

TABLE IX—Continued
CONDENSATIONS WITH KETONES

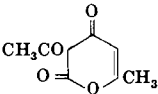
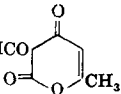
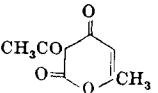
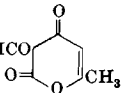
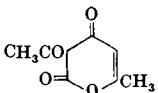
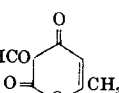
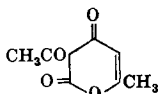
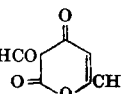
448

ORGANIC REACTIONS

THE KNOEVENAGEL CONDENSATION

449

C. Aromatic Aldehydes or Benzoylformanilide—Continued

Aldehyde or Ketone	Ketone	Catalyst	Temperature	Product(s) and Yield(s) (%)	Refs.
4-Isopropylbenzaldehyde (contd.)	Tetrahydrothiopyran-4-one	Piperidinium acetate	Boiling C ₂ H ₅ OH	4-(CH ₃) ₂ CHC ₆ H ₄ CH=CHC(=O)CHC ₆ H ₄ CH(CH ₃) ₂ -4 (31)	942
1-Naphthaldehyde		Piperidine	Boiling CHCl ₃	1-C ₁₀ H ₇ CH=CHCO-  (62)	939
	Tetrahydro-γ-pyrone	Piperidinium acetate	Boiling C ₂ H ₅ OH	1-C ₁₀ H ₇ CH=CHC(=O)CHC ₁₀ H ₇ -1 (58)	942
	Tetrahydrothiopyran-4-one	"	"	1-C ₁₀ H ₇ CH=CHC(=O)CHC ₁₀ H ₇ -1 (75)	942
4-Diethylaminobenzaldehyde		Piperidine	Boiling CHCl ₃	4-(C ₂ H ₅) ₂ NC ₆ H ₄ CH=CHCO-  (58)	939
3,4-Diethoxybenzaldehyde		"	"	3,4-(C ₂ H ₅ O) ₂ C ₆ H ₃ CH=CHCO-  (43)	939
Biphenyl-4-carboxaldehyde	N-Methyl-4-piperidone	"	Boiling C ₂ H ₅ OH	4-C ₆ H ₅ C ₆ H ₄ CH=CHC(=O)CHC ₆ H ₄ C ₆ H ₅ -4 (72)	167
Benzoylformanilide	Acetophenone	(C ₂ H ₅) ₂ NH/C ₂ H ₅ OH	Room	C ₆ H ₅ COCH ₂ C(C ₆ H ₅)(OH)CONHC ₆ H ₅ (85)	946
	4-Bromoacetophenone	"	"	4-BrC ₆ H ₄ COCH ₂ C(C ₆ H ₅)(OH)CONHC ₆ H ₅ (85)	946
D. Heterocyclic Aldehydes					
Pyrrole-2-carboxaldehyde	2-Hydroxyacetophenone	Piperidine	Boiling C ₂ H ₅ OH	2-C ₄ H ₃ NHCH=CHCOC ₆ H ₄ OH-2 (25)	947
Furfural	Biacetyl	Piperidine or piperidinium acetate in methanol	Room	2-C ₄ H ₃ OCH=CHCOCOCCH=CHC ₄ H ₃ O-2 (Small)	938,948
	Cycloheptane-1,2-dione	Piperidine	Boiling C ₂ H ₅ OH	2-C ₄ H ₃ OCH=CHC(=O)C ₇ H ₁₀ O-2 (28)	166
		"	Boiling CHCl ₃	2-C ₄ H ₃ OCH=CHCO-  (85)	939

Note: References 285 to 1153 are on pp. 582-599.

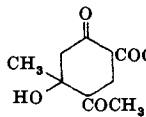
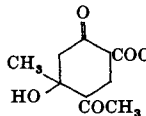
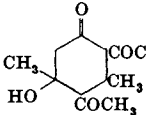
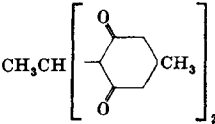
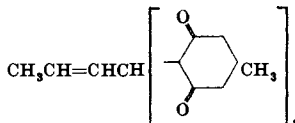
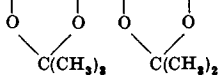
TABLE IX—Continued
CONDENSATIONS WITH KETONES

D. Heterocyclic Aldehydes—Continued

Aldehyde or Ketone	Ketone	Catalyst	Temperature	Product(s) and Yield(s) (%)	Refs.
Thiophene-2-carboxaldehyde		Piperidine	Boiling CHCl ₃	2-C ₄ H ₃ SCH=CHCO (—)	939
β-2-Furylacrolein	Biacetyl	Piperidine/C ₄ H ₉ OH	Room	2-C ₄ H ₃ O(CH=CH) ₂ COCO(CH=CH) ₂ C ₄ H ₃ O·2 (—)	948
Indole-3-carboxaldehyde	Acetophenone	Piperidine	175°	(59)	237
	4-Methylaceto-phenone	"	175°	(61)	237
	4-Methoxyaceto-phenone	"	175°	(60)	237
2-Furylpentadienal	Biacetyl	Piperidine/C ₄ H ₉ OH	Room	2-C ₄ H ₃ O(CH=CH) ₂ COCO(CH=CH) ₂ C ₄ H ₃ O·2 (—)	948
Quinoline-4-carboxaldehyde	Quinuclidone	Piperidinium acetate	Boiling C ₂ H ₅ OH	(—)	944
1-Methylindole-3-carboxaldehyde	Acetophenone	Piperidine	200°	(70)	237
	4-Methylaceto-phenone	"	200°	(80)	237
	4-Methoxyaceto-phenone	"	200°	(55)	237
2-Phenylindole-3-carboxaldehyde	Acetophenone	"	B.p.	(67)	923
	4-Methylaceto-phenone	"	B.p.	(67)	923
	4-Methoxyaceto-phenone	"	B.p.	(78)	923

Note: References 285 to 1153 are on pp. 582-599.

TABLE X
CONDENSATION WITH β -DIKETONES

A. Acyclic Aldehydes					
Aldehyde	β -Diketone	Catalyst	Temperature	Product(s) and Yield(s) (%)	Refs.
Formaldehyde	$\text{CH}_3\text{COCH}_2\text{COCH}_3$	$(\text{C}_2\text{H}_5)_2\text{NH}$	0–5°	 (50–60)	171, 172, 949
	"	None	Room	$\text{CH}_2[\text{CH}(\text{COCH}_3)_2]_2$ (82–87)	949
	"	$(\text{C}_2\text{H}_5)_2\text{NH}$	60–70°, then room	 (71)	172
	Dimedone	Piperidine	Boiling $\text{C}_2\text{H}_5\text{OH}$ or room	$\text{CH}_2\text{R}_2^{\dagger}$ (62)	169, 171
Glyoxal	$\text{C}_6\text{H}_5\text{COCH}_2\text{COC}_6\text{H}_5$	Piperidine/aq. ethanol	Room	$\text{CH}_2[\text{CH}(\text{COC}_6\text{H}_5)_2]_2$ (67)	171
	"	Piperidine/ $(\text{C}_2\text{H}_5)_2\text{O}$	Ice	$\text{CH}_2=\text{C}(\text{COC}_6\text{H}_5)_2$ (98)	173
	Dimedone	Piperidine	Boiling $\text{C}_2\text{H}_5\text{OH}$	$\text{R}_2\text{CHCHR}_2^{\dagger}$ (Good)	169
	Glyoxylic acid	"	"	$\text{HO}_2\text{CCHR}_2^{\dagger}$ (Good)	169
Acetaldehyde	$\text{CH}_3\text{COCH}_2\text{COCH}_3$	"	0°	 (89)	172, 949
	Dimedone	"	Boiling $\text{C}_2\text{H}_5\text{OH}$	$\text{CH}_3\text{CHR}_2^{\dagger}$ (Good)	169
	5-Methylcyclohexane-1,3-dione	"	"	 (85–95)	950
Acrolein	Dimedone	"	"	$\text{CH}_3=\text{CHCHR}_2^{\dagger}$ (Good)	169
Propionaldehyde	$\text{CH}_3\text{COCH}_2\text{COCH}_3$	$(\text{C}_2\text{H}_5)_2\text{NH}$	Room	$\text{CH}_3\text{CH}=\text{CHCH}(\text{COCH}_3)_2$ (43)	949
	Dimedone	Piperidine	Boiling $\text{C}_2\text{H}_5\text{OH}$	$\text{C}_2\text{H}_5\text{CHR}_2^{\dagger}$ (Good)	169
Crotonaldehyde	5-Methylcyclohexane-1,3-dione	"	"	 (85–95)	950
Ethyl glyoxylate	$\text{CH}_3\text{COCH}_2\text{COCH}_3$	Piperidine or $(\text{C}_2\text{H}_5)_2\text{NH}$	Room	$\text{C}_2\text{H}_5\text{O}_2\text{CCH}=\text{C}(\text{COCH}_3)_2$ (50)	951
<i>n</i> -Butyraldehyde	$\text{CH}_3\text{COCH}_2\text{COCH}_3$	Piperidine	"	$\text{CH}_3\text{CH}_2\text{CH}=\text{CHCH}(\text{COCH}_3)_2$ (85)	949
	Dimedone	"	Boiling $\text{C}_2\text{H}_5\text{OH}$	$n\text{-C}_3\text{H}_7\text{CHR}_2^{\dagger}$ (Good)	169
Isobutyraldehyde	Dimedone	"	"	$i\text{-C}_3\text{H}_7\text{CHR}_2^{\dagger}$ (Good)	169
4-Pentenal	Dimedone	"	Boiling $\text{C}_2\text{H}_5\text{OH}$	$\text{CH}_3=\text{CHCH}_2\text{CH}_2\text{CHR}_2^{\dagger}$ (Good)	169
Pentanal	Dimedone	"	"	$n\text{-C}_4\text{H}_9\text{CHR}_2^{\dagger}$ (Good)	169
3-Methylbutyraldehyde	Dimedone	"	"	$(\text{CH}_3)_2\text{CHCH}_2\text{CHR}_2^{\dagger}$ (Good)	169
Hexanal	Dimedone	"	"	$n\text{-C}_5\text{H}_{11}\text{CHR}_2^{\dagger}$ (Good)	169
Heptanal	$\text{CH}_3\text{COCH}_2\text{COCH}_3$	Piperidine/ethanol	Room	$n\text{-C}_6\text{H}_{13}\text{CH}[\text{CH}(\text{COCH}_3)_2]_2$ (54)	171
	Dimedone	Piperidine	Boiling $\text{C}_2\text{H}_5\text{OH}$	$n\text{-C}_6\text{H}_{13}\text{CHR}_2^{\dagger}$ (Good)	169
Octanal	Dimedone	"	"	$n\text{-C}_7\text{H}_{15}\text{CHR}_2^{\dagger}$ (Good)	169
Nonanal	Dimedone	"	"	$n\text{-C}_8\text{H}_{17}\text{CHR}_2^{\dagger}$ (Good)	169
Citronellal	Dimedone	"	"	$\text{CH}_2=\text{C}(\text{CH}_3)(\text{CH}_2)_5\text{CHR}_2^{\dagger}$ (Good)	169
Decanal	Dimedone	"	"	$n\text{-C}_9\text{H}_{19}\text{CHR}_2^{\dagger}$ (Good)	169
2,3,4,5-Diisopropylidene-D-arabinose	$\text{C}_6\text{H}_5\text{COCH}_2\text{COCH}_3$	$(\text{C}_2\text{H}_5)_2\text{NH}/\text{C}_6\text{H}_5\text{CH}_3$	0°	 (34)	174

Note: References 285 to 1153 are on pp. 582–599.

* This compound was reported to be $\text{CH}_2[\text{CH}(\text{COCH}_3)_2]_2$ in the earlier references.¹⁷²

† Paraformaldehyde was used in this reaction.


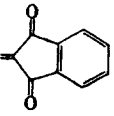
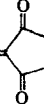
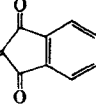
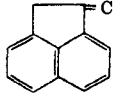
† R in this product represents the group — from dimedone (5,5-dimethylcyclohexane-1,3-dione).

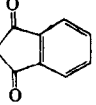
TABLE X—Continued
CONDENSATION WITH β -DIKETONES

454

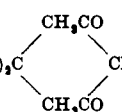
ORGANIC REACTIONS

B. <i>Alkyl Aldehydes or Ketones</i>					
Aldehyde	β -Diketone	Catalyst	Temperature	Product(s) and Yield(s) (%)	Refs.
Phenylacetaldehyde	Dimedone	Piperidine	Boiling C_2H_5OH	$C_6H_5CH_2CHR_2^\dagger$ (Good)	169
Cinnamaldehyde	$CH_3COCH_2COCH_3$	"	0°	$C_6H_5CH=CHCH[CH(COCH_3)_2]_2$ (—)	679
	"	Basic resins	—	$C_6H_5CH=CHCH=C(COCH_3)_2$ (—)	962
	Dimedone	Piperidine	Boiling C_2H_5OH	$C_6H_5CH=CHCHR_2^\dagger$ (Good)	169
4-Methoxy-cinnamaldehyde	Indan-1,3-dione	"	"	$4-CH_3OC_6H_4CH=CHCH$  (—)	953
2-Dimethylamino-cinnamaldehyde	Cyclopentane-1,3-dione	Piperidinium acetate	"	$2-(CH_3)_2NC_6H_4CH=CHCH$  (—)	760
	Indan-1,3-dione	"	"	$2-(CH_3)_2NC_6H_4CH=CHCH$  (—)	760
Acenaphthenone	$CH_3COCH_2COCH_3$	Piperidine	—	 $C(COCH_3)_2$ (—)	952
4-Phenyl-cinnamaldehyde	$CH_3COCH_2COCH_3$	"	—	$4-C_6H_5C_6H_4CH=CHCH=C(COCH_3)_2$ (—)	952

THE KNOEVENAGEL CONDENSATION

C. <i>Aromatic Aldehydes</i>					
2-Chlorobenzaldehyde	$CH_3COCH_2COCH_3$	Piperidine/ aq. C_2H_5OH	Room	$2-ClC_6H_4CH[CH(COCH_3)_2]_2$ (57)	171
3-Nitrobenzaldehyde	Dimedone	Piperidine	Boiling C_2H_5OH	$2-ClC_6H_4CHR_2^\dagger$ (Good)	169
	$CH_3COCH_2COCH_3$	"	Room	$3-O_2NC_6H_4CH=C(COCH_3)_2$ (85-90)	954
	$C_6H_5COCH_2COCH_3$	Piperidine/ C_2H_5OH	0°	$3-O_2NC_6H_4CH[CH(COCH_3)_2]COC_6H_5$ (—)	954
	Dimedone	Piperidine	Boiling C_2H_5OH	$3-O_2NC_6H_4CHR_2^\dagger$ (Good)	169
4-Nitrobenzaldehyde	Indan-1,3-dione	—	"	$4-O_2NC_6H_4CH$  (—)	191
Benzaldehyde	Dimedone	Piperidine	"	$4-O_2NC_6H_4CHR_2^\dagger$ (Good)	169
	$CH_3COCH_2COCH_3$	"	—10° to 0°	$C_6H_5CH=C(COCH_3)_2$ (66)	4, 955
	"	Piperidine + $n-C_8H_{17}CO_2H$	Boiling C_6H_6	$C_6H_5CH=C(COCH_3)_2$ (67)	69
	"	Piperidine/ aq. ethanol	Room	$C_6H_5CH[CH(COCH_3)_2]_2$ (49)	171
	1-Methoxypentane-2,4-dione	"	"	$C_6H_5CH[CH(COCH_3)COCH_2OCH_3]_2$ (9)	171
	Dimedone	Piperidine	Boiling C_2H_5OH	$C_6H_5CHR_2^\dagger$ (Good)	169
	$C_6H_5COCH_2COCH_3$	Piperidine/ aq. ethanol	Room	$C_6H_5CH[CH(COCH_3)COC_6H_5]_2$ (46)	171
	$C_6H_5COCH_2COC_6H_5$	Piperidine + $n-C_8H_{17}CO_2H$	Boiling C_6H_6	$C_6H_5CH=C(COC_6H_5)_2$ (61)	69
	Ethyl benzoyl-pyruvate	Piperidine	Warm	$C_6H_5CH[CH(COC_6H_5)COCO_2C_2H_5]_2$ (—)	3

Note: References 285 to 1153 are on pp. 582-599.

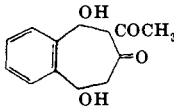
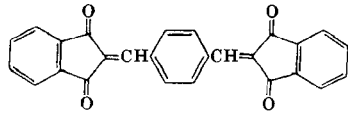
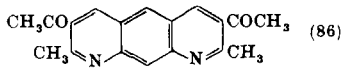
† R in this product represents the group  from dimedone (5,5-dimethylcyclohexane-1,3-dione).

455

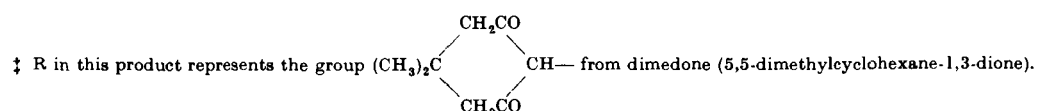
TABLE X—Continued
CONDENSATION WITH β -DIKETONES

456

ORGANIC REACTIONS

C. Aromatic Aldehydes—Continued					
Aldehyde	β -Diketone	Catalyst	Temperature	Product(s) and Yield(s) (%)	Refs.
Salicylaldehyde	$\text{CH}_3\text{COCH}_2\text{COCH}_3$	Piperidine	Ice/salt	$2\text{-HOC}_6\text{H}_4\text{CH}=\text{C}(\text{COCH}_3)_2$ (—)	170
	"	Basic resins	—	$2\text{-HOC}_6\text{H}_4\text{CH}=\text{C}(\text{COCH}_3)_2$ (—)	952
4-Hydroxybenzaldehyde	Dimedone	Piperidine	Boiling $\text{C}_2\text{H}_5\text{OH}$	$2\text{-HOC}_6\text{H}_4\text{CHR}_2^\dagger$ (Good)	169
	Dimedone	"	"	$4\text{-HOC}_6\text{H}_4\text{CHR}_2^\dagger$ (Good)	169
	1-Methoxypentane-2,4-dione	Piperidine/aq. ethanol	Room	$4\text{-HOC}_6\text{H}_4\text{CH}[\text{CH}(\text{COCH}_3)\text{COCH}_2\text{OCH}_3]_2$ (17)	171
2,4-Dihydroxybenzaldehyde	Dimedone	Piperidine	Boiling $\text{C}_2\text{H}_5\text{OH}$	$2,4\text{-(HO)}_2\text{C}_6\text{H}_3\text{CHR}_2^\dagger$ (Good)	169
3,4-Dihydroxybenzaldehyde (protocatechuic aldehyde)	Dimedone	"	"	$3,4\text{-(HO)}_2\text{C}_6\text{H}_3\text{CHR}_2^\dagger$ (Good)	169
Phthalaldehyde	$\text{CH}_3\text{COCH}_2\text{COCH}_3$	$(\text{C}_2\text{H}_5)_2\text{NH}$	50° , then room	 (85)	176
Terephthalaldehyde	Indan-1,3-dione	None	Boiling $\text{C}_2\text{H}_5\text{OH}$	 (Quant.)	191
Piperonal	$\text{CH}_3\text{COCH}_2\text{COCH}_3$	Piperidine/aq. ethanol	Room	$3,4\text{-CH}_2\text{O}_2\text{C}_6\text{H}_3\text{CH}[\text{CH}(\text{COCH}_3)_2]_2$ (52)	171
	Dimedone	Piperidine	Boiling $\text{C}_2\text{H}_5\text{OH}$	$3,4\text{-CH}_2\text{O}_2\text{C}_6\text{H}_3\text{CHR}_2^\dagger$ (Good)	169
	1-Methoxypentane-2,4-dione	Piperidine/aq. ethanol	Room	$3,4\text{-CH}_2\text{O}_2\text{C}_6\text{H}_3\text{CH}[\text{CH}(\text{COCH}_3)\text{COCH}_2\text{OCH}_3]_2$ (6)	171
2-Methylbenzaldehyde	Dimedone	Piperidine	Boiling $\text{C}_2\text{H}_5\text{OH}$	$2\text{-CH}_3\text{C}_6\text{H}_4\text{CHR}_2^\dagger$ (Good)	169
4-Methylbenzaldehyde	Dimedone	"	"	$4\text{-CH}_3\text{C}_6\text{H}_4\text{CHR}_2^\dagger$ (Good)	169
2-Methoxybenzaldehyde	$\text{CH}_3\text{COCH}_2\text{COCH}_3$	Piperidine/aq. ethanol	Room	$2\text{-CH}_3\text{OC}_6\text{H}_4\text{CH}[\text{CH}(\text{COCH}_3)_2]_2$ (54)	171
	Dimedone	Piperidine	Boiling $\text{C}_2\text{H}_5\text{OH}$	$2\text{-CH}_3\text{OC}_6\text{H}_4\text{CHR}_2^\dagger$ (Good)	169
4-Methoxybenzaldehyde (anisaldehyde)	$\text{CH}_3\text{COCH}_2\text{COCH}_3$	Piperidine/aq. ethanol	Room	$4\text{-CH}_3\text{OC}_6\text{H}_4\text{CH}[\text{CH}(\text{COCH}_3)_2]_2$ (77)	171
	Dimedone	Piperidine	Boiling $\text{C}_2\text{H}_5\text{OH}$	$4\text{-CH}_3\text{OC}_6\text{H}_4\text{CHR}_2^\dagger$ (Good)	169
	1-Methoxypentane-2,4-dione	Piperidine/aq. ethanol	Room	$4\text{-CH}_3\text{OC}_6\text{H}_4\text{CH}[\text{CH}(\text{COCH}_3)\text{COCH}_2\text{OCH}_3]_2$ (4)	171
2-Hydroxy-3-methoxybenzaldehyde (orthovanillin)	Dimedone	Piperidine	Boiling $\text{C}_2\text{H}_5\text{OH}$	$2\text{-HO-3-CH}_3\text{OC}_6\text{H}_3\text{CHR}_2^\dagger$ (Good)	169
3-Methoxy-4-hydroxybenzaldehyde (vanillin)	$\text{CH}_3\text{COCH}_2\text{COCH}_3$	$(\text{C}_2\text{H}_5)_2\text{NH}$	$50\text{--}60^\circ$	$3\text{-CH}_3\text{O-4-HOC}_6\text{H}_3\text{CH}=\text{C}(\text{COCH}_3)_2$ (85–90)	702
	"	"	90°	$3\text{-CH}_3\text{O-4-HOC}_6\text{H}_3\text{CH}[\text{CH}(\text{COCH}_3)_2]_2$ (80)	702
	"	Basic resins	—	$3\text{-CH}_3\text{O-4-HOC}_6\text{H}_3\text{CH}=\text{C}(\text{COCH}_3)_2$ (—)	952
	Dimedone	Piperidine	Boiling $\text{C}_2\text{H}_5\text{OH}$	$3\text{-CH}_3\text{O-4-HOC}_6\text{H}_3\text{CHR}_2^\dagger$ (Good)	169
4,6-Diaminoisophthalaldehyde	$\text{CH}_3\text{COCH}_2\text{COCH}_3$	"	$180\text{--}190^\circ$	 (86)	177
4-Dimethylaminobenzaldehyde	$\text{CH}_3\text{COCH}_2\text{COCH}_3$	Piperidine/aq. ethanol	Room	$4\text{-(CH}_3)_2\text{NC}_6\text{H}_4\text{CH}[\text{CH}(\text{COCH}_3)_2]_2$ (45)	171
	Dimedone	Piperidine	Boiling $\text{C}_2\text{H}_5\text{OH}$	$4\text{-(CH}_3)_2\text{NC}_6\text{H}_4\text{CHR}_2^\dagger$ (Good)	169
	1-Methoxypentane-2,4-dione	Piperidine/aq. ethanol	Room	$4\text{-(CH}_3)_2\text{NC}_6\text{H}_4\text{CH}[\text{CH}(\text{COCH}_3)\text{COCH}_2\text{OCH}_3]_2$ (35)	171

Note: References 285 to 1153 are on pp. 582–599.



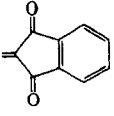
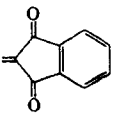
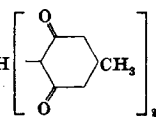
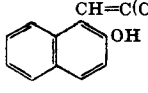
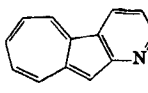
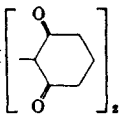
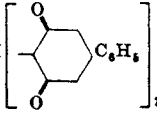
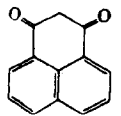
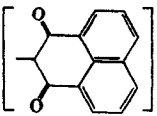
THE KNOEVENAGEL CONDENSATION

457

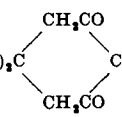
TABLE X—Continued
CONDENSATION WITH β -DIKETONES

458

ORGANIC REACTIONS

C. Aromatic Aldehydes—Continued					
Aldehyde	β -Diketone	Catalyst	Temperature	Product(s) and Yield(s) (%)	Refs.
4-Dimethylamino-benzaldehyde (<i>contd.</i>)	Indan-1,3-dione	Piperidine hydrochloride/ethanol	—	4-(CH ₃) ₂ NC ₆ H ₄ CH=  (—)	893
	"	Piperidinium acetate	Boiling C ₆ H ₅ OH	4-(CH ₃) ₂ NC ₆ H ₄ CH=  (—)	894
2,3-Dimethoxy-benzaldehyde	Dimedone	Piperidine	"	2,3-(CH ₃ O) ₂ C ₆ H ₃ CHR ₂ † (Good)	169
3,4-Dimethoxy-benzaldehyde	CH ₃ COCH ₂ COCH ₃	"	—	3,4-(CH ₃ O) ₂ C ₆ H ₃ CH=C(COCH ₃) ₂ (—)	952
(veratraldehyde)	Dimedone	"	Boiling C ₂ H ₅ OH	3,4-(CH ₃ O) ₂ C ₆ H ₃ CHR ₂ † (Good)	169
3-Methoxy-4-acetoxy-benzaldehyde (acetylvanillin)	"	"	"	3-CH ₃ O-4-CH ₃ CO ₂ C ₆ H ₃ CHR ₂ † (Good)	169
4-Isopropyl-benzaldehyde (cuminal)	CH ₃ COCH ₂ COCH ₃	"	—	4-i-C ₃ H ₇ C ₆ H ₄ CH=C(COCH ₃) ₂ (—)	952
	Dimedone	"	Boiling C ₂ H ₅ OH	4-i-C ₃ H ₇ C ₆ H ₄ CHR ₂ (Good)	169
3,4,5-Trimethoxy-benzaldehyde	5-Methylcyclohexane-1,3-dione	"	"	3,4,5-(CH ₃ O) ₃ C ₆ H ₂ CH  (85–95)	950
2-Hydroxy-1-naphthaldehyde	CH ₃ COCH ₂ COCH ₃	"	Cooled	 CH=C(COCH ₃) ₂ (96)	81
2-Aminoazulene-1-carboxaldehyde	CH ₃ COCH ₂ COCH ₃	"	Water bath	 COCH ₃ (50)	717, 718
4-Di-(2'-chloroethyl)-aminobenzaldehyde	Cyclohexane-1,3-dione	Piperazine	Boiling dioxane	4-(ClCH ₂ CH ₂) ₂ NC ₆ H ₄ CH  (57)	714
	Dimedone	"	"	4-(ClCH ₂ CH ₂) ₂ NC ₆ H ₄ CHR ₂ † (79)	714
	5-Phenylcyclohexane-1,3-dione	"	"	4-(ClCH ₂ CH ₂) ₂ NC ₆ H ₄ CH  (75)	714
		Piperidine	"	4-(ClCH ₂ CH ₂) ₂ NC ₆ H ₄ CH  (69)	714

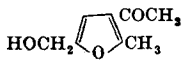
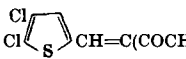

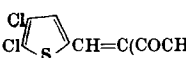

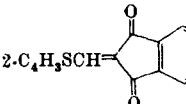
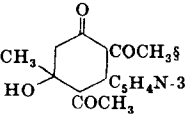
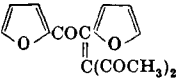
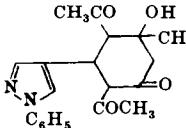
Note: References 285 to 1153 are on pp. 582–599.

† R in this product represents the group  from dimedone (5,5-dimethylcyclohexane-1,3-dione).

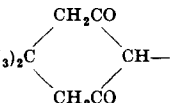
THE KNOEVENAGEL CONDENSATION

459

TABLE X—Continued
CONDENSATION WITH β -DIKETONES

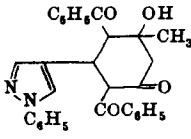
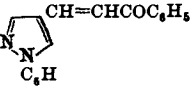
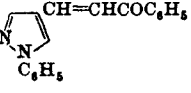
C. Aromatic Aldehydes—Continued					
Aldehyde	β -Diketone	Catalyst	Temperature	Product(s) and Yield(s) (%)	Refs.
2,3-Dibenzoyloxy-benzaldehyde	Dimedone	Piperidine	Boiling dioxane	2,3-(C ₆ H ₅ CH ₂ O) ₂ C ₆ H ₃ CHR ₂ [†] (78)	956
D. Heterocyclic Aldehydes					
Glycidaldehyde	CH ₃ COCH ₂ COCH ₃	Piperidinium acetate	Room, then steam bath	 (81)	175
4,5-Dichlorothiophene-2-carboxaldehyde	CH ₃ COCH ₂ COCH ₃	Piperidine	−15°	 (25)	
				 (27)	578
	C ₆ H ₅ COCH ₂ COCH ₃	„	20°	 (45)	578
				 (25)	
Furfural Thiophene-2-carboxaldehyde	CH ₃ COCH ₂ COCH ₃	„	Room	2-C ₄ H ₃ OCH=C(COCH ₃) ₂ (70)	957
	CH ₃ COCH ₂ COCH ₃	„	—	2-C ₄ H ₃ SCH=C(COCH ₃) ₂ (—)	952
	Indan-1,3-dione	Piperidine/C ₂ H ₅ OH	Room	 (—)	958
Pyridine-2-carboxaldehyde	CH ₃ COCH ₂ COCH ₃	Piperidine/ aq. C ₂ H ₅ OH	„	2-C ₅ H ₄ NCH[CH(COCH ₃) ₂] ₂ (28)	171
	1-Methoxypentane-2,4-dione	„	„	2-C ₅ H ₄ NCH[CH(COCH ₃)COCH ₂ OCH ₃] ₂ (26)	171
Pyridine-3-carboxaldehyde	CH ₃ COCH ₂ COCH ₃	„	„	 (96)	171, 949
Pyridine-4-carboxaldehyde	CH ₃ COCH ₂ COCH ₃	„	„	4-C ₅ H ₄ NCH[CH(COCH ₃) ₂] ₂ (47)	171
	1-Methoxypentane-2,4-dione	„	„	4-C ₅ H ₄ NCH[CH(COCH ₃)COCH ₂ OCH ₃] ₂ (58)	171
3-(2'-Furyl)acrolein	CH ₃ COCH ₂ COCH ₃	Basic resins	—	2-C ₄ H ₃ OCH=CHCH=C(COCH ₃) ₂ (—)	952
Furil	CH ₃ COCH ₂ COCH ₃	Piperidine	Boiling C ₂ H ₅ OH	 (—)	734
1-Phenylpyrazole-4-carboxaldehyde	CH ₃ COCH ₂ COCH ₃	Piperidine/C ₂ H ₅ OH	Room	 (72)	959

Note: References 285 to 1153 are on pp. 582–599.

[†] R in this product represents the group  from dimedone (5,5-dimethylcyclohexane-1,3-dione).

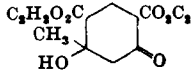
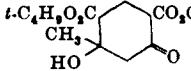
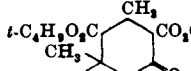
[§] This compound was originally reported as 3-C₅H₄NCH[CH(COCH₃)₂]₂.¹⁷¹

TABLE X—Continued
CONDENSATION WITH β -DIKETONES

D. Heterocyclic Aldehydes—Continued					
Aldehyde	β -Diketone	Catalyst	Temperature	Product(s) and Yield(s) (%)	Refs.
1-Phenylpyrazole-4-carboxaldehyde (<i>contd.</i>)	$C_6H_5COCH_2COCH_3$	Piperidine/ C_6H_5OH	Heat, then room	 (13)	959
				 (70)	
	$C_6H_5COCH_2COC_6H_5$	„	40–50°, then room	 (52)	959

Note: References 285 to 1153 are on pp. 582–599.

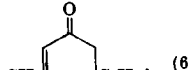
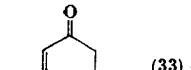
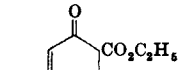
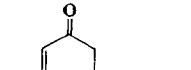
TABLE XI
CONDENSATIONS WITH β -KETONIC ESTERS

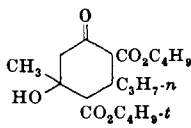
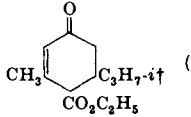
A. Acyclic Aldehydes or Ketones					
Aldehyde or Ketone	β -Ketonic Ester	Catalyst	Temperature	Product(s) and Yield(s) (%)	Refs.
Formaldehyde	$\text{CH}_3\text{COCH}_2\text{CO}_2\text{C}_2\text{H}_5$	$(\text{C}_2\text{H}_5)_3\text{NH}$	0°	 (—)	3, 959
	$\text{CH}_3\text{COCH}_2\text{CO}_2\text{C}_4\text{H}_9$	Piperidine/ $\text{C}_2\text{H}_5\text{OH}$	0°, then room	 (64)	960
Acetaldehyde	$\text{C}_2\text{H}_5\text{COCH}_2\text{CO}_2\text{C}_2\text{H}_5$	Aqueous $(\text{C}_2\text{H}_5)_3\text{NH}$	Cold	$\text{CH}_3[\text{CH}(\text{CO}_2\text{C}_2\text{H}_5)\text{COCH}_2\text{C}_2\text{H}_5]_2$ (—)	3
	$\text{CH}_3\text{COCH}_2\text{CO}_2\text{C}_2\text{H}_5$	Piperidine, $(\text{C}_2\text{H}_5)_3\text{NH}$, or $(n\text{-C}_3\text{H}_7)_3\text{N}$	"	$\text{CH}_3\text{CH}[\text{CH}(\text{CO}_2\text{C}_2\text{H}_5)\text{COCH}_3]_2$ (—)	3, 14, 185
	"	Piperidine	Ice	$\text{CH}_3\text{CH}=\text{C}(\text{CO}_2\text{C}_2\text{H}_5)\text{COCH}_3$ (75–80)	6
	"	Amberlite IR-4B or Deacidite	—	$\text{CH}_3\text{CH}=\text{C}(\text{CO}_2\text{C}_2\text{H}_5)\text{COCH}_3$ (51)	181
	$\text{CH}_3\text{COCH}_2\text{CO}_2\text{C}_4\text{H}_9$	Piperidine	0°, then room	 (65)	960
Propionaldehyde	Menthyl acetoacetate	Piperidine, $(\text{C}_2\text{H}_5)_3\text{NH}$, or $(n\text{-C}_3\text{H}_7)_3\text{N}$	–5°, then –15° Room	$\text{CH}_3\text{CH}=\text{C}(\text{CO}_2\text{C}_4\text{H}_9)\text{COCH}_3$ (62) $\text{CH}_3\text{CH}[\text{CH}(\text{CO}_2\text{C}_{10}\text{H}_{19})\text{COCH}_3]_2$ (—)	961 14
	$\text{CH}_3\text{COCH}_2\text{CO}_2\text{C}_2\text{H}_5$	$(\text{C}_2\text{H}_5)_3\text{NH}$	"	$\text{C}_2\text{H}_5\text{CH}[\text{CH}(\text{CO}_2\text{C}_2\text{H}_5)\text{COCH}_3]_2$ (—)	962

Note: References 285 to 1153 are on pp. 582–599.

* This compound was originally reported to be $\text{CH}_3[\text{CH}(\text{CO}_2\text{C}_2\text{H}_5)\text{COCH}_3]_2$.

TABLE XI—Continued
CONDENSATIONS WITH β -KETONIC ESTERS

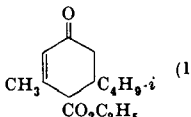
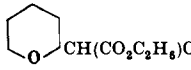
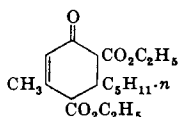
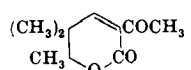
A. Acyclic Aldehydes or Ketones—Continued					
Aldehyde or Ketone	β -Ketonic Ester	Catalyst	Temperature	Product(s) and Yield(s) (%)	Refs.
Propionaldehyde (<i>contd.</i>)	$\text{CH}_3\text{COCH}_2\text{CO}_2\text{C}_2\text{H}_5$	Piperidine/ $\text{C}_2\text{H}_5\text{OH}$	Ice, then room	 (61)	185
	"	Weak base resins	—	$\text{C}_2\text{H}_5\text{CH}=\text{C}(\text{CO}_2\text{C}_2\text{H}_5)\text{COCH}_3$ (37)	181
	"	"	80–90°	$\text{C}_2\text{H}_5\text{CH}=\text{C}(\text{CO}_2\text{C}_2\text{H}_5)\text{COCH}_3$ (8)	180
	Menthyl acetoacetate	Piperidine in alcohol	Room	 (33) +  (4)	14
Ethyl glyoxylate	$\text{CH}_3\text{COCH}_2\text{CO}_2\text{C}_2\text{H}_5$	Piperidine or $(\text{C}_2\text{H}_5)_3\text{NH}$	"	$\text{C}_2\text{H}_5\text{CH}[\text{CH}(\text{CO}_2\text{C}_{10}\text{H}_{19})\text{COCH}_3]_2$ (—) or $\text{C}_2\text{H}_5\text{O}_2\text{CCH}=\text{C}(\text{CO}_2\text{C}_2\text{H}_5)\text{COCH}_3$ (60)	951
<i>n</i> -Butyraldehyde	$\text{CH}_3\text{COCH}_2\text{CO}_2\text{C}_2\text{H}_5$	Piperidine/ $\text{C}_2\text{H}_5\text{OH}$	Room	$n\text{-C}_3\text{H}_7\text{CH}=\text{C}(\text{CO}_2\text{C}_2\text{H}_5)\text{COCH}_3$ (81)	182
	"	Piperidinium acetate or CH_3CONH_2	Boiling C_6H_6	$n\text{-C}_3\text{H}_7\text{CH}=\text{C}(\text{CO}_2\text{C}_2\text{H}_5)\text{COCH}_3$ (52)	182
"	"	Piperidine/ $\text{C}_2\text{H}_5\text{OH}$	Ice, then room	 (64)	185

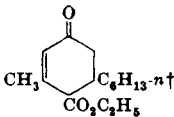
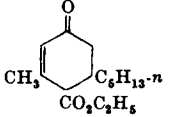
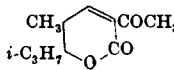
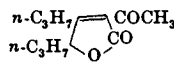
	$\text{CH}_3\text{COCH}_2\text{CO}_2\text{C}_3\text{H}_7$, <i>i</i>	Weak base resins Piperidine/ $\text{C}_2\text{H}_5\text{OH}$	Room or 80–90° Below 10°	$n\text{-C}_3\text{H}_7\text{CH}=\text{C}(\text{CO}_2\text{C}_2\text{H}_5)\text{COCH}_3$ (50) $n\text{-C}_3\text{H}_7\text{CH}=\text{C}(\text{CO}_2\text{C}_3\text{H}_7\text{-}i)\text{COCH}_3$ (75)	181 182
	$\text{CH}_3\text{COCH}_2\text{CO}_2\text{C}_4\text{H}_9$, <i>t</i>	"	0°, then room	 (63)	960
Isobutyraldehyde	Menthyl acetoacetate $\text{CH}_3\text{COCH}_2\text{CO}_2\text{C}_2\text{H}_5$	" " $(\text{C}_2\text{H}_5)_2\text{NH}/\text{C}_2\text{H}_5\text{OH}$	–5° to –15° Room Cold	$n\text{-C}_3\text{H}_7\text{CH}=\text{C}(\text{CO}_2\text{C}_4\text{H}_9\text{-}t)\text{COCH}_3$ (66) $n\text{-C}_3\text{H}_7\text{CH}[\text{CH}(\text{CO}_2\text{C}_{10}\text{H}_{19})\text{COCH}_3]_2$ (—) $i\text{-C}_3\text{H}_7\text{CH}[\text{CH}(\text{CO}_2\text{C}_2\text{H}_5)\text{COCH}_3]_2$ (—)	961 14 178
	"	Piperidine/ $\text{C}_2\text{H}_5\text{OH}$	Ice, then room	 (61)	185
	"	Amberlite IR-4B or Deacidite	—	$i\text{-C}_3\text{H}_7\text{CH}=\text{C}(\text{CO}_2\text{C}_2\text{H}_5)\text{COCH}_3$ (60)	181
Methyl ethyl ketone	$\text{CH}_3\text{COCH}_2\text{CO}_2\text{C}_4\text{H}_9$, <i>t</i>	Piperidine/ $\text{C}_2\text{H}_5\text{OH}$	–5°, then 70–80°	$i\text{-C}_3\text{H}_7\text{CH}=\text{C}(\text{CO}_2\text{C}_4\text{H}_9\text{-}t)\text{COCH}_3$ (78)	961
	Menthyl acetoacetate $\text{CH}_3\text{COCH}_2\text{CO}_2\text{C}_2\text{H}_5$	"	Room	$i\text{-C}_3\text{H}_7\text{CH}[\text{CH}(\text{CO}_2\text{C}_{10}\text{H}_{19})\text{COCH}_3]_2$ (—)	14
	"	"	Below 10°	None	182
Pentanal	"	Piperidinium acetate	Boiling benzene	None	182
	$\text{CH}_3\text{COCH}_2\text{CO}_2\text{C}_2\text{H}_5$	Amberlite IR-4B or deacidite	—	$n\text{-C}_4\text{H}_9\text{CH}=\text{C}(\text{CO}_2\text{C}_2\text{H}_5)\text{COCH}_3$ (60)	181
3-Methylbutanal	$\text{CH}_3\text{COCH}_2\text{CO}_2\text{C}_2\text{H}_5$	$(\text{C}_2\text{H}_5)_2\text{NH}$ or piperidine	0°	$i\text{-C}_4\text{H}_9\text{CH}[\text{CH}(\text{CO}_2\text{C}_2\text{H}_5)\text{COCH}_3]_2$ (—)	178
	"	Piperidine	0°	$i\text{-C}_4\text{H}_9\text{CH}=\text{C}(\text{CO}_2\text{C}_2\text{H}_5)\text{COCH}_3$ (83)	182, 963
	"	Piperidinium acetate or CH_3CONH_2	Boiling C_6H_6	$i\text{-C}_4\text{H}_9\text{CH}=\text{C}(\text{CO}_2\text{C}_2\text{H}_5)\text{COCH}_3$ (67)	182

Note: References 285 to 1153 are on pp. 582–599.

† The crude product was boiled with acetic acid and sulfuric acid.

TABLE XI—Continued
CONDENSATIONS WITH β -KETONIC ESTERS

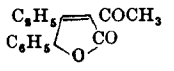
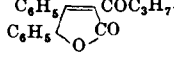
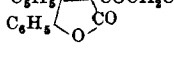
A. Acyclic Aldehydes or Ketones—Continued					
Aldehyde or Ketone	β -Ketonc Ester	Catalyst	Temperature	Product(s) and Yield(s) (%)	Refs.
3-Methylbutanal (contd.)	$\text{CH}_3\text{COCH}_2\text{CO}_2\text{C}_2\text{H}_5$	Weak base resins	80–90°	$i\text{-C}_4\text{H}_9\text{CH}=\text{C}(\text{CO}_2\text{C}_2\text{H}_5)\text{COCH}_3$ (35)	180
				 (10)	
	$\text{CH}_3\text{COCH}_2\text{CO}_2\text{C}_3\text{H}_7$, <i>i</i>	Piperidine/ $\text{C}_2\text{H}_5\text{OH}$	Below 10°	$i\text{-C}_4\text{H}_9\text{CH}=\text{C}(\text{CO}_2\text{C}_3\text{H}_7\text{-}i)\text{COCH}_3$ (89)	182
5-Hydroxypentanal	$\text{CH}_3\text{COCH}_2\text{CO}_2\text{C}_2\text{H}_5$	Piperidine	Boiling C_6H_6	 (79)	964
Hexanal	$\text{CH}_3\text{COCH}_2\text{CO}_2\text{C}_2\text{H}_5$	Weak base resins	100°	$n\text{-C}_5\text{H}_{11}\text{CH}=\text{C}(\text{CO}_2\text{C}_2\text{H}_5)\text{COCH}_3$ (8)	675
				 (40)	
2-Ethylbutyraldehyde	$\text{CH}_3\text{COCH}_2\text{CO}_2\text{C}_2\text{H}_5$	Piperidine/ $\text{C}_2\text{H}_5\text{OH}$	Below 10°	$(\text{C}_2\text{H}_5)_2\text{CHCH}=\text{C}(\text{CO}_2\text{C}_2\text{H}_5)\text{COCH}_3$ (71)	182
	"	Piperidinium acetate	Boiling C_6H_6	$(\text{C}_2\text{H}_5)_2\text{CHCH}=\text{C}(\text{CO}_2\text{C}_2\text{H}_5)\text{COCH}_3$ (63)	182
	"	Amberlite IR-4B or Deacidite	—	$(\text{C}_2\text{H}_5)_2\text{CHCH}=\text{C}(\text{CO}_2\text{C}_2\text{H}_5)\text{COCH}_3$ (64)	181
2,2-Dimethyl-3-hydroxybutyr-aldehyde	$\text{CH}_3\text{COCH}_2\text{CO}_2\text{CH}_3$	Piperidinium acetate	Boiling xylene	 (—)	965
Heptanal	$\text{CH}_3\text{COCH}_2\text{CO}_2\text{C}_2\text{H}_5$	Piperidine	0°	$n\text{-C}_6\text{H}_{13}\text{CH}[\text{CH}(\text{CO}_2\text{C}_2\text{H}_5)\text{COCH}_3]_2$ (—)	178
	"	"	0°	$n\text{-C}_6\text{H}_{13}\text{CH}=\text{C}(\text{CO}_2\text{C}_2\text{H}_5)\text{COCH}_3$ (80–85)	963

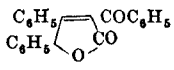
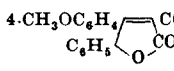
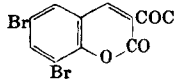
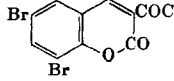
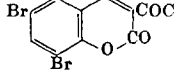
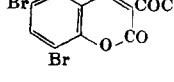
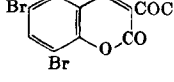
		Piperidine/C ₂ H ₅ OH	Ice, then room	 (71)	185
		Amberlite IR-4B or Deacidite	—	$n\text{-C}_8\text{H}_{17}\text{CH}=\text{C}(\text{CO}_2\text{C}_2\text{H}_5)\text{COCH}_3$ (51)	181
		Weak base resins	100°	$n\text{-C}_8\text{H}_{17}\text{CH}=\text{C}(\text{CO}_2\text{C}_2\text{H}_5)\text{COCH}_3$ (30)	180
				 (15)	
Methyl <i>n</i> -pentyl ketone	CH ₃ COCH ₂ CO ₂ C ₂ H ₅	Piperidine/C ₂ H ₅ OH	Below 10°	None	182
		Piperidinium acetate	Boiling C ₆ H ₆	None	182
2,4-Dimethyl-3-hydroxypentanal	CH ₃ COCH ₂ CO ₂ CH ₃		Boiling CH ₃ CO ₂ H	 (57)	186, 965
2-Ethylhexanal	CH ₃ COCH ₂ CO ₂ C ₂ H ₅	Piperidine/C ₂ H ₅ OH	Below 10°	$n\text{-C}_8\text{H}_{17}\text{CH}(\text{C}_2\text{H}_5)\text{CH}=\text{C}(\text{CO}_2\text{C}_2\text{H}_5)\text{COCH}_3$ (72)	182
		Piperidinium acetate	Boiling C ₆ H ₆	$n\text{-C}_8\text{H}_{17}\text{CH}(\text{C}_2\text{H}_5)\text{CH}=\text{C}(\text{CO}_2\text{C}_2\text{H}_5)\text{COCH}_3$ (64)	182
		Amberlite IR-4B or Deacidite	—	$n\text{-C}_8\text{H}_{17}\text{CH}(\text{C}_2\text{H}_5)\text{CH}=\text{C}(\text{CO}_2\text{C}_2\text{H}_5)\text{COCH}_3$ (58)	181
4-Hydroxyoctan-3-one	CH ₃ COCH ₂ CO ₂ CH ₃	Pyridine + CH ₃ CO ₂ H	Boiling xylene	 (67)	186, 965

Note: References 285 to 1153 are on pp. 582–599.

† The crude product was boiled with acetic acid and sulfuric acid.

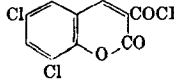
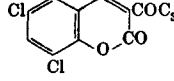
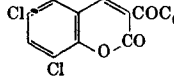
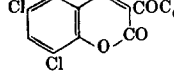
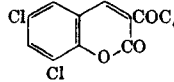
TABLE XI—Continued
CONDENSATIONS WITH β -KETONIC ESTERS

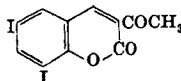
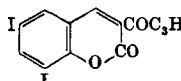
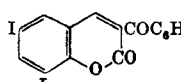
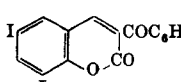
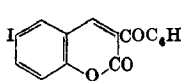
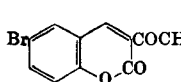
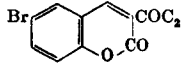
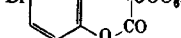
A. Acyclic Aldehydes or Ketones—Continued					
Aldehyde or Ketone	β -Ketonic Ester	Catalyst	Temperature	Product(s) and (Yields) (%)	Refs.
Citral	Acetoacetic acid CH ₃ COCH ₂ CO ₂ C ₂ H ₅	Pyridine Piperidine hydrochloride	Heat 60°	Pseudoionone (—) (CH ₃) ₂ C=CHCH ₂ CH ₂ C(CH ₃)=CHCH=C(CO ₂ C ₂ H ₅)COCH ₃ (—)	8 791
2,3,4,5-Diisopropylidene-D-arabinose	CH ₃ COCH ₂ CO ₂ C ₂ H ₅	(C ₂ H ₅) ₂ NH/ C ₆ H ₅ CH ₃	0°	2,3,4,5-Diisopropylidene-D-arabino-sylideneacetoacetic ester (74)	174
B. Aromatic Aldehydes or Ketones					
Cinnamaldehyde	CH ₃ COCH ₂ CO ₂ C ₂ H ₅	(C ₂ H ₅) ₂ NH or piperidine	—	C ₆ H ₅ CH=CHCH[CH(CO ₂ C ₂ H ₅)COCH ₃] ₂ (—)	3
2-Hydroxy-4-methoxyacetophenone	CH ₃ COCH ₂ CO ₂ C ₂ H ₅	Piperidine Piperidine/ C ₆ H ₅ CH ₃	0° Cold, then hot	C ₆ H ₅ CH=CHCH=C(CO ₂ C ₂ H ₅)COCH ₃ (40)	963 966
β -(2,5-Dimethoxyphenyl)propionaldehyde	CH ₃ COCH ₂ CO ₂ C ₂ H ₅	Piperidine	0°	2,5-(CH ₃ O) ₂ C ₆ H ₃ CH ₂ CH ₂ CH[CH(COCH ₃)-CO ₂ C ₂ H ₅] ₂ (69)	964
Benzoin	CH ₃ COCH ₂ CO ₂ CH ₃		Boiling C ₆ H ₅ CH ₃	 (56)	186, 965
Methyl 3-ketohexanoate		Pyridine + CH ₃ CO ₂ H	—	 (—)	965
Methyl 4-phenyl-3-ketobutyrate		Piperidinium acetate	Boiling xylene	 (—)	965

	$C_6H_5COCH_2CO_2CH_3$	„	„	 (30)	965
4-Methoxybenzoin	$CH_3COCH_2CO_2CH_3$	„	„	 (39)	965
<i>C. Aromatic Aldehydes</i>					
3,5-Dibromobenzaldehyde	$CH_3COCH_2CO_2C_2H_5$	Piperidine	—	$3,5-Br_2C_6H_3CH=CH(CO_2C_2H_5)COCH_3$ (—)	967
3,5-Dibromosalicylaldehyde	$CH_3COCH_2CO_2C_2H_5$	Piperidine/alcohol	17°	 (60)	281, 967 968
	Ethyl 3-ketohexanoate	Piperidine/ C_2H_5OH	Room	 (85)	281
	$C_6H_5COCH_2CO_2C_2H_5$	„	28°	 (98)	969
	$4-CH_3OC_6H_4COCH_2CO_2C_2H_5$	Piperidine	Room	 (—)	719
	Ethyl 2-thenoyl acetate	Piperidine/ C_2H_5OH	„	 (74)	281

Note: References 285 to 1153 are on pp. 582-599.

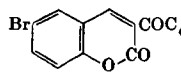
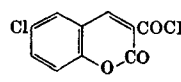
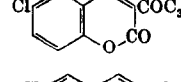
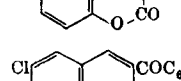
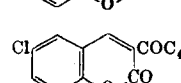
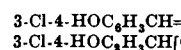
TABLE XI—Continued
CONDENSATIONS WITH β -KETONIC ESTERS

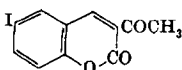
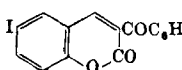
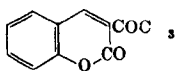
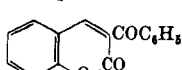
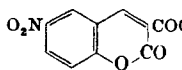
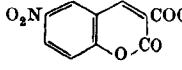
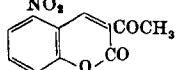
<i>C. Aromatic Aldehydes—Continued</i>					
Aldehyde	β -Ketonic Ester	Catalyst	Temperature	Product(s) and Yield(s) (%)	Refs.
3,4-Dichlorobenzaldehyde	$CH_3COCH_2CO_2C_2H_5$	Piperidine	—	$3,4-Cl_2C_6H_3CH[CH(CO_2C_2H_5)COCH_3]_2$ (—)	967
3,5-Dichlorobenzaldehyde	$CH_3COCH_2CO_2C_2H_5$	„	—	$3,5-Cl_2C_6H_3CH=CH(CO_2C_2H_5)COCH_3$ (—)	967
3,5-Dichlorosalicylaldehyde	$CH_3COCH_2CO_2C_2H_5$	„	17°	 (88)	281, 968
	Ethyl 3-ketohexanoate	„	Room	 (90)	281
	$C_6H_5COCH_2CO_2C_2H_5$	Piperidine/alcohol	28°	 (100)	969
	$4-CH_3OC_6H_4COCH_2CO_2C_2H_5$	Piperidine	Room	 (—)	719
	Ethyl 2-thenoylacetate	„	„	 (90)	281
3,5-Diodobenzaldehyde	$CH_3COCH_2CO_2C_2H_5$	„	—	$3,5-I_2C_6H_3CH=CH(CO_2C_2H_5)COCH_3$	967

3,5-Diiodosalicyl- aldehyde	$\text{CH}_3\text{COCH}_2\text{CO}_2\text{C}_2\text{H}_5$	„	28°	 (86)	967, 968
Ethyl 3-ketohexanoate	„	Room	 (45)	281	
$\text{C}_6\text{H}_5\text{COCH}_2\text{CO}_2\text{C}_2\text{H}_5$	Piperidine/alcohol	30°	 (98)	969	
4- $\text{CH}_3\text{OC}_6\text{H}_4\text{COCH}_2\text{CO}_2\text{C}_2\text{H}_5$	Piperidine	Room	 (—)	719	
Ethyl 2-thenoylacetate	„	„	 (60)	281	
5-Bromosalicyl- aldehyde	$\text{CH}_3\text{COCH}_2\text{CO}_2\text{C}_2\text{H}_5$	„	„	 (98)	281, 968
Ethyl 3-ketohexanoate	„	„	 (90)	281	
$\text{C}_6\text{H}_5\text{COCH}_2\text{CO}_2\text{C}_2\text{H}_5$	„	28°	 (100)	969	

Note: References 285 to 1153 are on pp. 582-599.

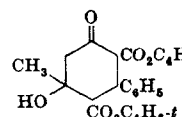
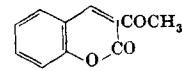
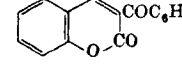
TABLE XI—Continued
CONDENSATIONS WITH β -KETONIC ESTERS

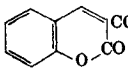
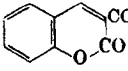
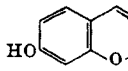
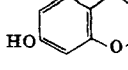
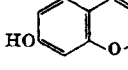
C. Aromatic Aldehydes—Continued					
Aldehyde	β -Ketonic Ester	Catalyst	Temperature	Product(s) and Yield(s) (%)	Refs.
5-Bromosalicyl-aldehyde (<i>contd.</i>)	Ethyl 2-thenoylacetate	Piperidine	Room	 (74)	281
3-Bromo-4-hydroxy-benzaldehyde	$\text{CH}_2\text{COCH}_2\text{CO}_2\text{C}_2\text{H}_5$	"	—	3-Br-4-HOC ₆ H ₃ CH=C(CO ₂ C ₂ H ₅)COCH ₃ (—)	967
4-Chlorobenzaldehyde	$\text{CH}_3\text{COCH}_2\text{CO}_2\text{C}_2\text{H}_5$	(C ₂ H ₅) ₂ NH/alcohol Piperidine	Room "	4-ClC ₆ H ₄ CH[CH(CO ₂ C ₂ H ₅)COCH ₃] ₂ (86) 4-ClC ₆ H ₄ CH=C(CO ₂ C ₂ H ₅)COCH ₃ (85)	970 958, 967
5-Chlorosalicyl-aldehyde	$\text{CH}_3\text{COCH}_2\text{CO}_2\text{C}_2\text{H}_5$	"	"	 (100)	967, 968
	Ethyl 3-ketohexanoate	"	"	 (—)	281
	$\text{C}_6\text{H}_5\text{COCH}_2\text{CO}_2\text{C}_2\text{H}_5$	Piperidine/alcohol	28°	 (100)	969
	4-CH ₃ OC ₆ H ₄ COCH ₂ - CO ₂ C ₂ H ₅	Piperidine	Room	 (90)	719
	Ethyl 2-thenoylacetate	Piperidine/C ₂ H ₅ OH	Room	 (—)	281
3-Chloro-4-hydroxy-benzaldehyde	$\text{CH}_3\text{COCH}_2\text{CO}_2\text{C}_2\text{H}_5$	Piperidine	—	3-Cl-4-HOC ₆ H ₃ CH=C(CO ₂ C ₂ H ₅)COCH ₃ (—) 3-Cl-4-HOC ₆ H ₃ CH[CH(CO ₂ C ₂ H ₅)COCH ₃] ₂ (—)	967

5-Iodosalicylaldehyde	$\text{CH}_3\text{COCH}_2\text{CO}_2\text{C}_2\text{H}_5$	Piperidine/alcohol	28°	 (98)	968
	$\text{C}_6\text{H}_5\text{COCH}_2\text{CO}_2\text{C}_2\text{H}_5$	"	30°	 (100)	969
2-Nitrobenzaldehyde	$\text{CH}_3\text{COCH}_2\text{CO}_2\text{C}_2\text{H}_5$	$(\text{C}_2\text{H}_5)_2\text{NH}$	Room	$2\text{-O}_2\text{NC}_6\text{H}_4\text{CH}[\text{CH}(\text{CO}_2\text{C}_2\text{H}_5)\text{COCH}_3]_2$ (Small)	970
3-Nitrobenzaldehyde	$\text{CH}_3\text{COCH}_2\text{CO}_2\text{C}_2\text{H}_5$	Piperidine	"	$3\text{-O}_2\text{NC}_6\text{H}_4\text{CH}[\text{CH}(\text{CO}_2\text{C}_2\text{H}_5)\text{COCH}_3]_2$ (Quant.)	970
	"	"	0°	$3\text{-O}_2\text{NC}_6\text{H}_4\text{CH}=\text{C}(\text{CO}_2\text{C}_2\text{H}_5)\text{COCH}_3$ (—)	963
4-Nitrobenzaldehyde	$\text{C}_6\text{H}_5\text{COCH}_2\text{CO}_2\text{C}_2\text{H}_5$	Piperidine/alcohol	Room	$3\text{-O}_2\text{NC}_6\text{H}_4\text{CH}=\text{C}(\text{CO}_2\text{C}_2\text{H}_5)\text{COC}_6\text{H}_5$ (—)	688
	$\text{CH}_3\text{COCH}_2\text{CO}_2\text{C}_2\text{H}_5$	Piperidine	"	$4\text{-O}_2\text{NC}_6\text{H}_4\text{CH}[\text{CH}(\text{CO}_2\text{C}_2\text{H}_5)\text{COCH}_3]_2$ (78)	970
3-Nitrosalicyl-aldehyde	$\text{CH}_3\text{COCH}_2\text{CO}_2\text{C}_2\text{H}_5$	Piperidine/alcohol	15°	 (80)	968
	$\text{C}_6\text{H}_5\text{COCH}_2\text{CO}_2\text{C}_2\text{H}_5$	"	30°	 (82)	969
5-Nitrosalicyl-aldehyde	$\text{CH}_3\text{COCH}_2\text{CO}_2\text{C}_2\text{H}_5$	Piperidine/ $\text{C}_6\text{H}_5\text{OH}$	Room	 (88)	968, 971
	$\text{C}_6\text{H}_5\text{COCH}_2\text{CO}_2\text{C}_2\text{H}_5$	Piperidine/alcohol	30°	 (93)	969
6-Nitrosalicyl-aldehyde	$\text{CH}_3\text{COCH}_2\text{CO}_2\text{C}_2\text{H}_5$	Piperidine/ $\text{C}_2\text{H}_5\text{OH}$	—	 (57)	971

Note: References 285 to 1153 are on pp. 582-599.

TABLE XI—Continued
CONDENSATIONS WITH β -KETONIC ESTERS

C. Aromatic Aldehydes—Continued					
Aldehyde	β -Ketonic Ester	Catalyst	Temperature	Product(s) and Yield(s) (%)	Refs.
Benzaldehyde	$\text{CH}_3\text{COCH}_2\text{CO}_2\text{C}_2\text{H}_5$	$(\text{C}_2\text{H}_5)_2\text{NH}$ or piperidine	Room	$\text{C}_6\text{H}_5\text{CH}[\text{CH}(\text{CO}_2\text{C}_2\text{H}_5)\text{COCH}_3]_2$ (Quant.)	3
+	"	$(\text{C}_2\text{H}_5)_2\text{NH}$	0°	$\text{C}_6\text{H}_5\text{CH}=\text{C}(\text{CO}_2\text{C}_2\text{H}_5)\text{COCH}_3$ (95)	5
	"	None	0°	$\text{C}_6\text{H}_5\text{CH}=\text{C}(\text{CO}_2\text{C}_2\text{H}_5)\text{COCH}_3$ (Quant.)	963
	"	$(n\text{-C}_3\text{H}_7)_3\text{N}$	Room	$\text{C}_6\text{H}_5\text{CH}[\text{CH}(\text{CO}_2\text{C}_2\text{H}_5)\text{COCH}_3]_2$ (—)	14
	"	Piperidine	Boiling C_6H_6	$\text{C}_6\text{H}_5\text{CH}=\text{C}(\text{CO}_2\text{C}_2\text{H}_5)\text{COCH}_3$ (83)	69
	"	+ $n\text{-C}_6\text{H}_{11}\text{CO}_2\text{H}$	Room or warm	$\text{C}_6\text{H}_5\text{CH}=\text{C}(\text{CO}_2\text{C}_2\text{H}_5)\text{COCH}_3$ (40)	181, 675
	"	Weak base resins			973
	$\text{CH}_3\text{COCH}_2\text{CO}_2\text{C}_4\text{H}_9\text{-}t$	Piperidine/ $\text{C}_2\text{H}_5\text{OH}$	—5°	$\text{C}_6\text{H}_5\text{CHOHCH}(\text{CO}_2\text{C}_4\text{H}_9\text{-}t)\text{COCH}_3$ § (70)	961
	Menthyl acetoacetate	Piperidine/alcohol	Water bath	$\text{C}_6\text{H}_5\text{CH}=\text{C}(\text{CO}_2\text{C}_{10}\text{H}_{19})\text{COCH}_3$ (—)	14
	$i\text{-C}_3\text{H}_7\text{COCH}_2\text{CO}_2\text{C}_2\text{H}_5$	Piperidine	Room	$\text{C}_6\text{H}_5\text{CH}[\text{CH}(\text{CO}_2\text{C}_2\text{H}_5)\text{COCH}_3]_2$ (—)	689
				$\text{C}_6\text{H}_5\text{CH}=\text{C}(\text{CO}_2\text{C}_2\text{H}_5)\text{COC}_6\text{H}_5\text{-}i$ (86)	
	$\text{CH}_3\text{COCH}_2\text{CO}_2\text{C}_4\text{H}_9\text{-}t$	Piperidine/ $\text{C}_2\text{H}_5\text{OH}$	0°, then room	 (50)	960
	$\text{C}_6\text{H}_5\text{COCH}_2\text{CO}_2\text{C}_2\text{H}_5$	$(\text{C}_2\text{H}_5)_2\text{NH}$	Cold	$\text{C}_6\text{H}_5\text{CH}[\text{CH}(\text{CO}_2\text{C}_2\text{H}_5)\text{COC}_6\text{H}_5]_2$ (—)	3, 688, 972
	"	Piperidine	Room	$\text{C}_6\text{H}_5\text{CH}=\text{C}(\text{CO}_2\text{C}_2\text{H}_5)\text{COC}_6\text{H}_5$ (—)	688
Salicylaldehyde	$\text{CH}_3\text{COCH}_2\text{CO}_2\text{C}_2\text{H}_5$	Piperidine/ $\text{C}_2\text{H}_5\text{OH}$	0° or room	 (Quant.)	963, 968, 971
	$\text{C}_6\text{H}_5\text{COCH}_2\text{CO}_2\text{C}_2\text{H}_5$	Piperidine	Cooled or room (30°)	 (100)	170, 869

	$4\text{-CH}_3\text{OC}_6\text{H}_4\text{COCH}_2\text{-CO}_2\text{C}_2\text{H}_5$..	Room	 $\text{COC}_6\text{H}_4\text{OCH}_3\cdot 4$ (—)	719
Salicylidene aniline	$\text{C}_6\text{H}_5\text{COCH}_2\text{CO}_2\text{C}_2\text{H}_5$	—	20°	 COC_6H_5 (—)	6
3-Hydroxybenzaldehyde	$\text{CH}_3\text{COCH}_2\text{CO}_2\text{C}_2\text{H}_5$..	Room	$3\text{-HOC}_6\text{H}_4\text{CH}=\text{C}(\text{CO}_2\text{C}_2\text{H}_5)\text{COCH}_3$ (86)	708, 974
	$\text{C}_6\text{H}_5\text{COCH}_2\text{CO}_2\text{C}_2\text{H}_5$	$3\text{-HOC}_6\text{H}_4\text{CH}[\text{CH}(\text{CO}_2\text{C}_2\text{H}_5)\text{COCH}_3]_2$ ¶ (98)	974
				$3\text{-HOC}_6\text{H}_4\text{CH}=\text{C}(\text{CO}_2\text{C}_2\text{H}_5)\text{COC}_6\text{H}_5$ (98)	974
				$3\text{-HOC}_6\text{H}_4\text{CH}[\text{CH}(\text{CO}_2\text{C}_2\text{H}_5)\text{COC}_6\text{H}_5]_2$ ¶ (98)	974
4-Hydroxybenzaldehyde	$\text{CH}_3\text{COCH}_2\text{CO}_2\text{C}_2\text{H}_5$	Piperidine/ $\text{C}_2\text{H}_5\text{OH}$..	$4\text{-HOC}_6\text{H}_4\text{CH}=\text{C}(\text{CO}_2\text{C}_2\text{H}_5)\text{COCH}_3$ (96)	974
	$\text{C}_6\text{H}_5\text{COCH}_2\text{CO}_2\text{C}_2\text{H}_5$	$4\text{-HOC}_6\text{H}_4\text{CH}[\text{CH}(\text{CO}_2\text{C}_2\text{H}_5)\text{COCH}_3]_2$ ¶ (98)	974
				$4\text{-HOC}_6\text{H}_4\text{CH}=\text{C}(\text{CO}_2\text{C}_2\text{H}_5)\text{COC}_6\text{H}_5$ (98)	974
2,4-Dihydroxybenzaldehyde (β -resorcyaldehyde)	$\text{CH}_3\text{COCH}_2\text{CO}_2\text{C}_2\text{H}_5$	Piperidine/alcohol	—5°	 COCH_3 (79)	968
	$\text{C}_6\text{H}_5\text{COCH}_2\text{CO}_2\text{C}_2\text{H}_5$..	—5°	 COC_6H_5 (98)	969
	Ethyl 2-thenoylacetate	Piperidine/ $\text{C}_2\text{H}_5\text{OH}$	Room	 $\text{COC}_6\text{H}_5\text{S}\cdot 2$ (75)	281
3,4-Dihydroxybenzaldehyde (protocatechuic aldehyde)	$\text{CH}_3\text{COCH}_2\text{CO}_2\text{C}_2\text{H}_5$	Piperidine + pyridine	..	$3,4\text{-(HO)}_2\text{C}_6\text{H}_3\text{CH}=\text{C}(\text{CO}_2\text{C}_2\text{H}_5)\text{COCH}_3$ (50–55)	975

Note: References 285 to 1153 are on pp. 582–599.

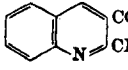
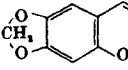
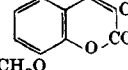
† The bis-piperide of benzaldehyde was used.

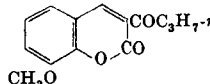
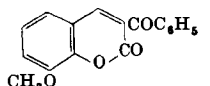
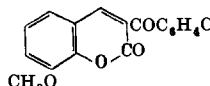
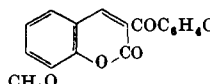
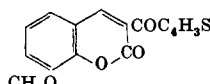
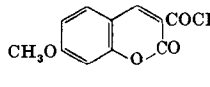
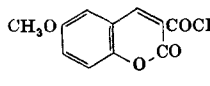
§ This compound was dehydrated slowly on standing to give $\text{C}_6\text{H}_5\text{CH}=\text{C}(\text{CO}_2\text{C}_2\text{H}_5)_2$.

|| Lower yields are reported with pyridine and lutidine.^{***}

¶ The β -ketonic ester in 100% excess was used.

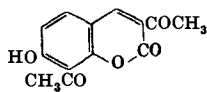
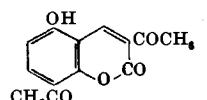
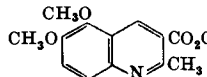
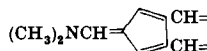
TABLE XI—Continued
CONDENSATIONS WITH β -KETONIC ESTERS

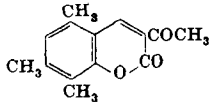
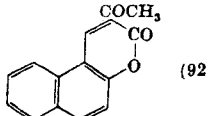
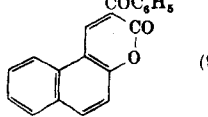
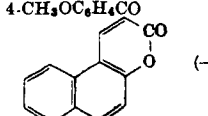
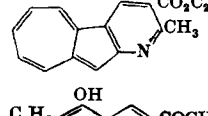
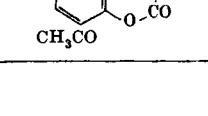
C. Aromatic Aldehydes—Continued					
Aldehyde	β -Ketonc Ester	Catalyst	Temperature	Product(s) and Yield(s) (%)	Refs.
3,4-Dihydroxybenzaldehyde (protocatechuic aldehyde) (contd.)	$\text{CH}_3\text{COCH}_2\text{CO}_2\text{C}_2\text{H}_5$ $\text{C}_6\text{H}_5\text{COCH}_2\text{CO}_2\text{C}_2\text{H}_5$	Piperidine/ $\text{C}_2\text{H}_5\text{OH}$..	Room ..	$3,4\text{-(HO)}_2\text{C}_6\text{H}_3\text{CH}=\text{C}(\text{CO}_2\text{C}_2\text{H}_5)\text{COCH}_3$ (86) $3,4\text{-(HO)}_2\text{C}_6\text{H}_3\text{CH}=\text{C}(\text{CO}_2\text{C}_2\text{H}_5)\text{COC}_6\text{H}_5$ (89)	974 974
2-Aminobenzaldehyde <i>p</i> -toluidide	$\text{CH}_3\text{COCH}_2\text{CO}_2\text{C}_2\text{H}_5$	Piperidine	Water bath	 $\text{CO}_2\text{C}_6\text{H}_4\text{CH}_3$ (50)	188
3,4-Methylenedioxybenzaldehyde (piperonal)	$\text{CH}_3\text{COCH}_2\text{CO}_2\text{C}_2\text{H}_5$..	$(\text{C}_2\text{H}_5)_3\text{NH}$ or piperidine Piperidinium acetate	Room Boiling C_2H_5	$3,4\text{-CH}_2\text{O}_2\text{C}_6\text{H}_3\text{CH}[\text{CH}(\text{CO}_2\text{C}_2\text{H}_5)\text{COCH}_3]_2$ (80) $3,4\text{-CH}_2\text{O}_2\text{C}_6\text{H}_3\text{CH}[\text{CH}(\text{CO}_2\text{C}_2\text{H}_5)\text{COCH}_3]_2$ (60)	183, 970 976
2-Hydroxy-4,5-methylenedioxybenzaldehyde	$\text{CH}_3\text{COCH}_2\text{CO}_2\text{C}_2\text{H}_5$	Piperidine	Boiling $\text{C}_2\text{H}_5\text{OH}$	 COCH_3 (95)	419
3-Bromo-4-hydroxy-5-methoxybenzaldehyde	$\text{CH}_3\text{COCH}_2\text{CO}_2\text{C}_2\text{H}_5$..	Room	$3\text{-Br-4-HO-5-CH}_2\text{OC}_6\text{H}_3\text{-CH}[\text{CH}(\text{CO}_2\text{C}_2\text{H}_5)\text{COCH}_3]_2$ (34)	179, 967
3-Methylbenzaldehyde	$\text{CH}_3\text{COCH}_2\text{CO}_2\text{C}_2\text{H}_5$	Piperidine/ $\text{C}_2\text{H}_5\text{OH}$..	$3\text{-CH}_3\text{C}_6\text{H}_4\text{CH}[\text{CH}(\text{CO}_2\text{C}_2\text{H}_5)\text{COCH}_3]_2$ (58)	977
2-Methoxybenzaldehyde	$\text{CH}_3\text{COCH}_2\text{CO}_2\text{C}_2\text{H}_5$	$(\text{C}_2\text{H}_5)_3\text{NH}$ or piperidine	..	$2\text{-CH}_3\text{OC}_6\text{H}_4\text{CH}[\text{CH}(\text{CO}_2\text{C}_2\text{H}_5)\text{COCH}_3]_2$ (56)	970, 977
4-Methoxybenzaldehyde (anisaldehyde)	$\text{CH}_3\text{COCH}_2\text{CO}_2\text{C}_2\text{H}_5$	Piperidine	..	$4\text{-CH}_3\text{OC}_6\text{H}_4\text{CH}[\text{CH}(\text{CO}_2\text{C}_2\text{H}_5)\text{COCH}_3]_2$ (74)	179, 970, 977
2-Hydroxy-3-methoxybenzaldehyde (orthovanillin)	$\text{CH}_3\text{COCH}_2\text{CO}_2\text{C}_2\text{H}_5$..	Room, or boiling $\text{C}_2\text{H}_5\text{OH}$	 COCH_3 (94)	146, 281

Ethyl 3-ketohexanoate	„	Room		(—)	281	
$C_6H_5COCH_2CO_2C_2H_5$	„	Boiling C_2H_5OH		(94)	146	
$2-ClC_6H_4COCH_2CO_2C_2H_5$	Piperidine/ C_2H_5OH	Room		(—)	281	
$4-CH_3OC_6H_4COCH_2CO_2C_2H_5$	Piperidine	„		(—)	719	
Ethyl 2-thenoylacetate	Piperidine/ C_2H_5OH	„		(84)	281	
2-Hydroxy-4-methoxybenzaldehyde	$CH_3COCH_2CO_2C_2H_5$	Piperidine	Boiling C_2H_5OH		(77)	978
2-Hydroxy-5-methoxybenzaldehyde	$CH_3COCH_2CO_2C_2H_5$	„	„		(70)	978
3-Methoxy-4-hydroxybenzaldehyde (vanillin)	$CH_3COCH_2CO_2C_2H_5$	Piperidine or $(C_2H_5)_2NH$	70°	$3-CH_3O-4-HOC_6H_3CH=C(CO_2C_2H_5)COCH_3$ (Quant.)	702	

Note: References 285 to 1153 are on pp. 582-599.

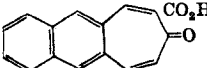
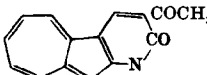
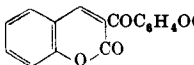
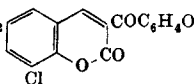
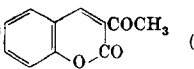
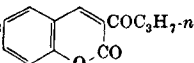
TABLE XI—Continued
CONDENSATIONS WITH β -KETONIC ESTERS

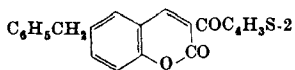
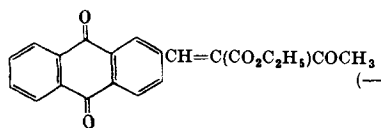
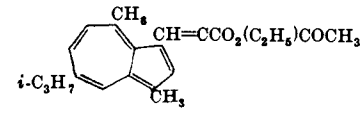
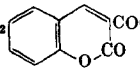
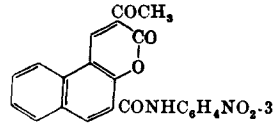
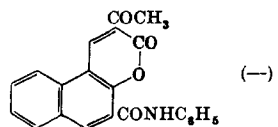
C. Aromatic Aldehydes—Continued					
Aldehyde	β -Ketonic Ester	Catalyst	Temperature	Product(s) and Yield(s) (%)	Refs.
2,4-Dihydroxy-3-acetylbenzaldehyde	$CH_3COCH_2CO_2C_2H_5$	Piperidine	Room	 (—)	703
2,6-Dihydroxy-3-acetylbenzaldehyde	$CH_3COCH_2CO_2C_2H_5$	„	„	 (35)	704
2,3-Dimethoxybenzaldehyde	$CH_3COCH_2CO_2C_2H_5$	Piperidine/ C_2H_5OH	„	$2,3-(CH_3O)_2C_6H_3CH[CH(CO_2C_2H_5)COCH_3]_2$ (68)	977
2,5-Dimethoxybenzaldehyde	$CH_3COCH_2CO_2C_2H_5$	Piperidine	0°	$2,5-(CH_3O)_2C_6H_3CH[CH(CO_2C_2H_5)COCH_3]_2$ (69)	964
3,4-Dimethoxybenzaldehyde (veratraldehyde)	$CH_3COCH_2CO_2C_2H_5$	Piperidinium acetate	Boiling C_6H_6	$3,4-(CH_3O)_2C_6H_3CH=C(CO_2C_2H_5)COCH_3$ (63)	976
2-Amino-5,6-dimethoxybenzaldehyde	$CH_3COCH_2CO_2C_2H_5$	Piperidine	Water bath	 (90)	187
6-Dimethylamino-fulvene-3,4-dicarboxaldehyde	$C_6H_5COCH_2CO_2C_2H_5$	„	Room	 (70)	711
4-Isopropylbenzaldehyde (cuminal)	$CH_3COCH_2CO_2C_2H_5$	„	0°	$4-(CH_3)_2CHC_6H_4CH=C(CO_2C_2H_5)COCH_3$ (90)	963
	„	$(C_2H_5)_2NH$	Room	$4-(CH_3)_2CHC_6H_4CH[CH(CO_2C_2H_5)COCH_3]_2$ (60-65)	970

2-Hydroxy-3,4,6-trimethylbenzaldehyde	$\text{CH}_3\text{COCH}_2\text{CO}_2\text{C}_2\text{H}_5$	Piperidine	"		(—)	979
3-Ethoxy-4-methoxybenzaldehyde	$\text{CH}_3\text{COCH}_2\text{CO}_2\text{C}_2\text{H}_5$	"	"	$3\text{-C}_2\text{H}_5\text{O-4-CH}_3\text{OC}_6\text{H}_3\text{-CH}[\text{CH}(\text{CO}_2\text{C}_2\text{H}_5)\text{COCH}_3]_2$ (56)		179
2-Hydroxy-1-naphthaldehyde	$\text{CH}_3\text{COCH}_2\text{CO}_2\text{C}_2\text{H}_5$	"	Water bath		(92)	81
	$\text{C}_6\text{H}_5\text{COCH}_2\text{CO}_2\text{C}_2\text{H}_5$	"	Room		(94)	81
	$4\text{-CH}_3\text{OC}_6\text{H}_4\text{COCH}_2\text{-CO}_2\text{C}_6\text{H}_5$	"	"		(—)	719
2-Aminoazulene-1-carboxaldehyde	$\text{CH}_3\text{COCH}_2\text{CO}_2\text{C}_2\text{H}_5$	"	Water bath		(35)	717, 718
3-Acetyl-2,6-dihydroxy-5-ethylbenzaldehyde	$\text{CH}_3\text{COCH}_2\text{CO}_2\text{C}_2\text{H}_5$	"	Room		(50)	703

Note: References 285 to 1153 are on pp. 582-599.

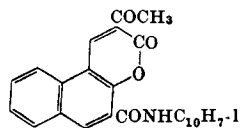
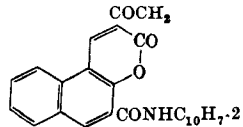
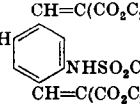
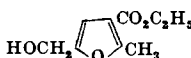
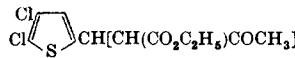
TABLE XI—Continued
CONDENSATIONS WITH β -KETONIC ESTERS






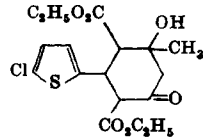
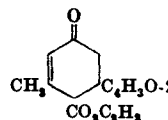
C. Aromatic Aldehydes—Continued					
Aldehyde	β -Ketonc Ester	Catalyst	Temperature	Product(s) and Yield(s) (%)	Refs.
3- <i>n</i> -Propoxy-4-methoxybenzaldehyde	$\text{CH}_3\text{COCH}_2\text{CO}_2\text{C}_2\text{H}_5$	"	"	3- <i>n</i> -C ₃ H ₇ O-4-CH ₃ OC ₆ H ₃ -CH[CH(CO ₂ C ₂ H ₅)COCH ₃] ₂ (64)	179
Naphthalene-2,3-dicarboxaldehyde	Acetoacetic acid	(C ₆ H ₅) ₃ NH	120–130°	 (—)	189
3-Methoxy-4- <i>n</i> -butoxybenzaldehyde	$\text{CH}_3\text{COCH}_2\text{CO}_2\text{C}_2\text{H}_5$	Piperidine	Room	3-CH ₃ O-4- <i>n</i> -C ₄ H ₉ OC ₆ H ₃ -CH[CH(CO ₂ C ₂ H ₅)COCH ₃] ₂ (67)	179
2-Acetamidoazulene-1-carboxaldehyde	$\text{CH}_3\text{COCH}_2\text{CO}_2\text{C}_2\text{H}_5$	"	Boiling C ₂ H ₅ OH	 (25)	717, 718
5-(3',4'-Dichlorobenzyl)salicylaldehyde	4-CH ₃ OC ₆ H ₄ COCH ₂ -CO ₂ C ₂ H ₅	"	Room	3,4-Cl ₂ C ₆ H ₃ CH ₂ -  (—)	719
3-Chloro-5-benzylsalicylaldehyde	4-CH ₃ OC ₆ H ₄ COCH ₂ -CO ₂ C ₂ H ₅	"	"	C ₆ H ₅ CH ₂ -  (—)	719
5-Benzylsalicylaldehyde	$\text{CH}_3\text{COCH}_2\text{CO}_2\text{C}_2\text{H}_5$	"	"	C ₆ H ₅ CH ₂ -  (—)	720
	Ethyl 3-ketohexanoate	"	"	C ₆ H ₅ CH ₂ -  (83)	281

	Ethyl 2-thenoylacetate	Piperidine/C ₂ H ₅ OH	„		(90)	281
Antraquinone-2-carboxaldehyde	CH ₃ COCH ₂ CO ₂ C ₂ H ₅	Piperidine	200°, then 180–190°		(—)	721
3-Benzoyloxy-4-methoxybenzaldehyde	CH ₃ COCH ₂ CO ₂ C ₂ H ₅	„	Room	3-C ₆ H ₄ CH ₂ O-4-CH ₃ OC ₆ H ₃ -CH[CH(CO ₂ C ₂ H ₅)COCH ₃] ₂	(70)	179
3-Methoxy-4-benzoyloxybenzaldehyde	CH ₃ COCH ₂ CO ₂ C ₂ H ₅	„	„	3-CH ₃ O-4-C ₆ H ₄ CH ₂ OC ₆ H ₃ -CH[CH(CO ₂ C ₂ H ₅)COCH ₃] ₂	(66)	179
3,8-Dimethyl-5-isopropylazulene-1-carboxaldehyde	CH ₃ COCH ₂ CO ₂ C ₂ H ₅	Piperidine/C ₂ H ₅ OH	„		(54)	568
5-(4'-Isopropylbenzyl)salicylaldehyde	4-CH ₃ OC ₆ H ₄ COCH ₂ CO ₂ C ₂ H ₅	Piperidine	„	4- <i>i</i> -C ₃ H ₇ C ₆ H ₄ CH ₂ -  -4	(—)	719
1-Formyl-2-hydroxy-naphthalene-3-carboxylic acid 3'-nitroanilide	CH ₃ COCH ₂ CO ₂ C ₂ H ₅	Piperidine + pyridine	Water bath		(—)	725
1-Formyl-2-hydroxy-naphthalene-3-carboxylic acid anilide	CH ₃ COCH ₂ CO ₂ C ₆ H ₅	„	„		(—)	725

Note: References 285 to 1153 are on pp. 582–599.

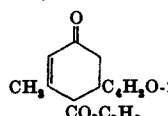
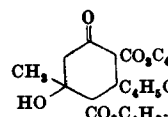
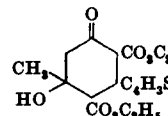
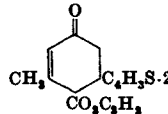
TABLE XI—Continued
CONDENSATIONS WITH β -KETONIC ESTERS

C. Aromatic Aldehydes—Continued					
Aldehyde	β -Ketonic Ester	Catalyst	Temperature	Product(s) and Yield(s) (%)	Refs.
1-Formyl-2-hydroxy-naphthalene-3-carboxylic acid 1'-naphthylamide	CH ₃ COCH ₂ CO ₂ C ₂ H ₅	Piperidine + pyridine	Water bath		(—) 725
1-Formyl-2-hydroxy-naphthalene-3-carboxylic acid 2'-naphthylamide	CH ₃ COCH ₂ CO ₂ C ₂ H ₅	„	„		(—) 725
2,6-Di- <i>p</i> -toluenesulfonamidoterephthalaldehyde	CH ₃ COCH ₂ CO ₂ C ₂ H ₅	Piperidine	70°	4-CH ₃ C ₆ H ₄ SO ₂ NH-  -4	(90) 230
D. Heterocyclic Aldehydes or Ketones					
Aldehyde or Ketone					
Glycidaldehyde	CH ₃ COCH ₂ CO ₂ C ₂ H ₅	Piperidinium acetate	40–50°		(67) 175
4,5-Dichlorothiophene-2-carboxaldehyde	CH ₃ COCH ₂ CO ₂ C ₂ H ₅	Piperidine	–5° to –10°		(47) 578

	$C_6H_5COCH_2CO_2C_2H_5$	„	-5°	 $CH=C(CO_2C_2H_5)COC_6H_5$ (48)	578
				 $CH[CH(CO_2C_2H_5)COC_6H_5]_2$ (10)	
				$C_6H_5COCH_3$ (14)	
5-Bromofurfural	$CH_3COCH_2CO_2C_2H_5$	„	Room	 $CH[CH(CO_2C_2H_5)COCH_3]_2$ (77)	183
5-Chlorofurfural	$CH_3COCH_2CO_2C_2H_5$	„	„	 $CH[CH(CO_2C_2H_5)COCH_3]_2$ (46)	183
5-Chlorothiophene-2-carboxaldehyde	$CH_3COCH_2CO_2C_2H_5$	„	„	 $CH[CH(CO_2C_2H_5)COCH_3]_2$ (70)	183
	„	„	„	 (—)	958
Furfural	$CH_3COCH_2CO_2C_2H_5$	„	0°	$2-C_6H_5OCH=C(CO_2C_2H_5)COCH_3$ (—)	963
	„	$(C_2H_5)_3NH$	$50-60^\circ$	 (56-64)	980

Note: References 285 to 1153 are on pp. 582-599.

TABLE XI—Continued
CONDENSATIONS WITH β -KETONIC ESTERS

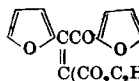
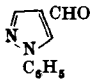
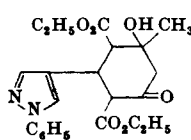
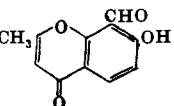
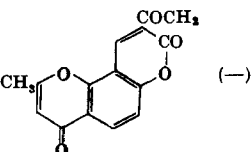
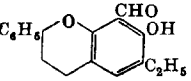
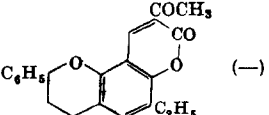
D. Heterocyclic Aldehydes or Ketones—Continued					
Aldehyde or Ketone	β -Ketonic Ester	Catalyst	Temperature	Product(s) and Yield(s) (%)	Refs.
Furfural (contd.)	$CH_3COCH_2CO_2C_2H_5$	Amberlite IR-4B, Deacidite, or AN-2F**	Room or warm	$2-C_6H_5OCH=C(CO_2C_2H_5)COCH_3$ (42)	181, 973
	„	Weak base resins	—	$2-C_6H_5OCH=C(CO_2C_2H_5)COCH_3$ (10)	675
				 C_6H_5O-2 (15)	
	$C_6H_5COCH_2CO_2C_2H_5$	Piperidine	-15°	$2-C_6H_5OCH=C(CO_2C_2H_5)COC_6H_5$ (30)	957
	$CH_3COCH_2CO_2C_6H_5$	Piperidine/ C_6H_5OH	0° , then room	 $CO_2C_6H_5$ -t C_6H_5O-2 (52)	960
	„	„	-8° , then -15°	$2-C_6H_5OCH=C(CO_2C_6H_5-t)COCH_3$ (64)	961
Thiophene-2-carboxaldehyde	$CH_3COCH_2CO_2C_2H_5$	Piperidine or piperidinium acetate	Room	 $CO_2C_2H_5$ C_6H_5S-2 (100)	184, 958
	„	$(C_2H_5)_3NH$	70°	 C_6H_5S-2 (85)	980

Pyrrole-2-carboxaldehyde	$\text{CH}_3\text{COCH}_2\text{CO}_2\text{C}_2\text{H}_5$	Piperidine	Room	$2\text{-C}_6\text{H}_5\text{SCH}[\text{CH}(\text{CO}_2\text{C}_2\text{H}_5)\text{COCH}_3]_2$ (51)	183
	$\text{CH}_3\text{COCH}_2\text{CO}_2\text{C}_2\text{H}_5$	Piperidine/ $\text{C}_2\text{H}_5\text{OH}$	-10°	$2\text{-C}_6\text{H}_5\text{SCH}=\text{C}(\text{CO}_2\text{C}_2\text{H}_5)\text{COCH}_3$ (68)	961
	$\text{CH}_3\text{COCH}_2\text{CO}_2\text{C}_2\text{H}_5$	Piperidine	Room	$2\text{-C}_6\text{H}_5\text{NCH}[\text{CH}(\text{CO}_2\text{C}_2\text{H}_5)\text{COCH}_3]_2$ (54)	183
Pyridine-2-carboxaldehyde	$\text{CH}_3\text{COCH}_2\text{CO}_2\text{C}_2\text{H}_5$	$(\text{C}_2\text{H}_5)_2\text{NH}$	Ice chest	$2\text{-C}_6\text{H}_5\text{NCH}=\text{C}(\text{CO}_2\text{C}_2\text{H}_5)\text{COCH}_3$ (86)	911
	$\text{CH}_3\text{COCH}_2\text{CO}_2\text{C}_2\text{H}_5$	Piperidine/ $(\text{C}_2\text{H}_5)_2\text{O}$	-20°	$2\text{-C}_6\text{H}_5\text{NCHOHCH}(\text{CO}_2\text{C}_2\text{H}_5)\text{COCH}_3$ (—)	981
Pyridine-3-carboxaldehyde	$\text{CH}_3\text{COCH}_2\text{CO}_2\text{C}_2\text{H}_5$	Piperidine	Room	$2\text{-C}_6\text{H}_5\text{NCH}=\text{C}(\text{CO}_2\text{C}_2\text{H}_5)\text{COCH}_3$ (58)	911
	$\text{CH}_3\text{COCH}_2\text{CO}_2\text{C}_2\text{H}_5$	"	"	$3\text{-C}_6\text{H}_5\text{NCH}[\text{CH}(\text{CO}_2\text{C}_2\text{H}_5)\text{COCH}_3]_2$ (60)	183
	"	Piperidine/ $(\text{C}_2\text{H}_5)_2\text{O}$	-20°	$3\text{-C}_6\text{H}_5\text{NCHOHCH}(\text{CO}_2\text{C}_2\text{H}_5)\text{COCH}_3$ (—)	981
5-Methylfurfural	$\text{CH}_3\text{COCH}_2\text{CO}_2\text{C}_2\text{H}_5$	Piperidine	Room	$\text{CH}_3\text{C}_4\text{H}_3\text{OCH}[\text{CH}(\text{CO}_2\text{C}_2\text{H}_5)\text{COCH}_3]_2$ (45)	183
5-Methylthiophene-2-carboxaldehyde	$\text{CH}_3\text{COCH}_2\text{CO}_2\text{C}_2\text{H}_5$	"	"	$\text{CH}_3\text{C}_4\text{H}_3\text{SCH}[\text{CH}(\text{CO}_2\text{C}_2\text{H}_5)\text{COCH}_3]_2$ (67)	183
5-Ethylthiophene-2-carboxaldehyde	$\text{CH}_3\text{COCH}_2\text{CO}_2\text{C}_2\text{H}_5$	"	"	$\text{C}_2\text{H}_5\text{C}_4\text{H}_3\text{SCH}[\text{CH}(\text{CO}_2\text{C}_2\text{H}_5)\text{COCH}_3]_2$ (34)	183
2,5-Dimethylthiophene-3-carboxaldehyde	$\text{CH}_3\text{COCH}_2\text{CO}_2\text{C}_2\text{H}_5$	"	"	$\text{CH}_3\text{C}_4\text{H}_2\text{SCH}[\text{CH}(\text{CO}_2\text{C}_2\text{H}_5)\text{COCH}_3]_2$ (68, 85)	183, 958
5-n-Propylthiophene-2-carboxaldehyde	$\text{CH}_3\text{COCH}_2\text{CO}_2\text{C}_2\text{H}_5$	"	"	$n\text{-C}_3\text{H}_7\text{C}_4\text{H}_3\text{SCH}[\text{CH}(\text{CO}_2\text{C}_2\text{H}_5)\text{COCH}_3]_2$ (24)	183

Note: References 285 to 1153 are on pp. 582-599.

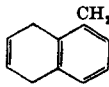
** AN-2F is a polyethylene polyamine formaldehyde polymer.

TABLE XI—Continued
CONDENSATIONS WITH β -KETONIC ESTERS

D. Heterocyclic Aldehydes or Ketones—Continued					
Aldehyde or Ketone	β -Ketonic Ester	Catalyst	Temperature	Product(s) and Yield(s) (%)	Refs.
Furil	$\text{CH}_3\text{COCH}_2\text{CO}_2\text{C}_2\text{H}_5$	Piperidine/alcohol	—	 (—)	734
Quinoline-2-carboxaldehyde	$\text{CH}_3\text{COCH}_2\text{CO}_2\text{C}_2\text{H}_5$	$(\text{C}_2\text{H}_5)_2\text{NH}$	Room	$2\text{-C}_{10}\text{H}_7\text{NCH}=\text{C}(\text{CO}_2\text{C}_2\text{H}_5)\text{COCH}_3$ (—)	190
Quinoline-6-carboxaldehyde	$\text{CH}_3\text{COCH}_2\text{CO}_2\text{C}_2\text{H}_5$	Piperidine/ $\text{C}_2\text{H}_5\text{OH}$ + $(\text{C}_2\text{H}_5)_2\text{O}$	0°	$6\text{-C}_{10}\text{H}_7\text{NCH}=\text{C}(\text{CO}_2\text{C}_2\text{H}_5)\text{COCH}_3$ (Low)	735
	$\text{CH}_3\text{COCH}_2\text{CO}_2\text{C}_2\text{H}_5$	Piperidine/ $\text{C}_2\text{H}_5\text{OH}$	Room	 (81)	959
	$\text{CH}_3\text{COCH}_2\text{CO}_2\text{C}_2\text{H}_5$	Piperidine	—	 (—)	738
	$\text{CH}_3\text{COCH}_2\text{CO}_2\text{C}_2\text{H}_5$	"	Room	 (—)	739

Note: References 285 to 1153 are on pp. 582-599.

TABLE XII
CONDENSATIONS WITH DIETHYL ACETONEDICARBOXYLATE

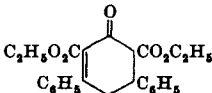
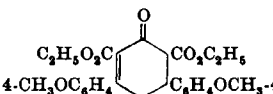
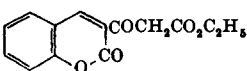
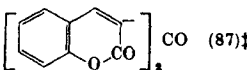
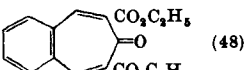
A. Acyclic Aldehydes				
Aldehyde	Catalyst	Temperature	Product(s) and Yield(s) (%)	Refs.
Formaldehyde	(C ₂ H ₅) ₂ NH	Ice	CH ₂ [CH(CO ₂ C ₂ H ₅)COCH ₂ CO ₂ C ₂ H ₅] ₂ (—)	178
i-C ₃ H ₇ CHO	"	"	i-C ₃ H ₇ CH[CH(CO ₂ C ₂ H ₅)COCH ₂ CO ₂ C ₂ H ₅] ₂ (—)	178
Heptanal	"	"	n-C ₆ H ₁₃ CH[CH(CO ₂ C ₂ H ₅)COCH ₂ CO ₂ C ₂ H ₅] ₂ (—)	178
1,2-O-Isopropylidene-D-xylopentadiol	Piperidine	Boiling C ₆ H ₆	R ₁ CH=C(CO ₂ C ₂ H ₅)COC(CO ₂ C ₂ H ₅)=CHR ₁ * (—)	192
4,6-O-Benzylidene-D-glucose	"	Boiling CH ₃ OH	R ₂ CH=C(CO ₂ C ₂ H ₅)COC(CO ₂ C ₂ H ₅)=CHR ₂ † (—)	192
2,3,4,5-Tetra-O-acetyl-D-galactadiol	"	Boiling aq. CH ₃ OH	$ \begin{array}{c} \text{CH}_3\text{CO}_2\text{CH}-\text{CH}=\text{CCO}_2\text{C}_2\text{H}_5 \\ \text{CH}_3\text{CO}_2\text{CH} \quad \quad \quad \text{C}=\text{O} \quad (-) \\ \text{CH}_3\text{CO}_2\text{CH} \\ \text{CH}_3\text{CO}_2\text{CH}-\text{CH}=\text{CCO}_2\text{C}_2\text{H}_5 \end{array} $	192
B. Alicyclic Aldehyde				
Cyclohexene-4,5-dicarboxaldehyde	Piperidinium acetate	Boiling C ₆ H ₆	 $\text{CH}=\text{C}(\text{CO}_2\text{C}_2\text{H}_5)\text{COCH}_2\text{CO}_2\text{C}_2\text{H}_5$ (—)	194

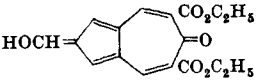
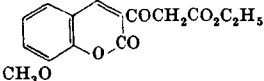
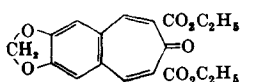
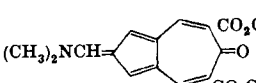
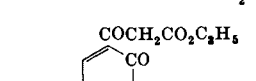
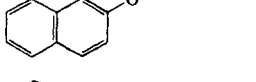
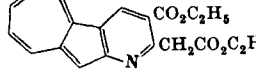
Note: References 285 to 1153 are on pp. 582-599.

* R₁ = 1,2-O-Isopropylidene-D-xylofuranosyl.

† R₂ = 4,6-O-Benzylidene-D-glucosyl.

TABLE XII—Continued
CONDENSATIONS WITH DIETHYL ACETONEDICARBOXYLATE

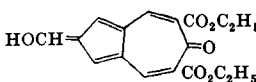
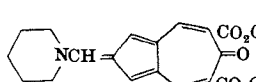
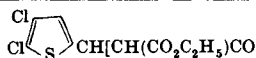
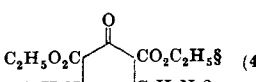
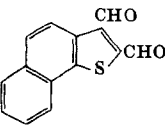
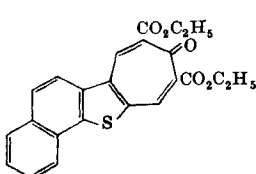
C. Aromatic Ketones				
Aldehyde or Ketone	Catalyst	Temperature	Product(s) and Yield(s) (%)	Refs.
C ₆ H ₅ CH=CHCOC ₆ H ₅	Piperidine/C ₂ H ₅ OH	40°	 (90-91)	196
4-CH ₃ OC ₆ H ₄ CH=CHCOC ₆ H ₄ OCH ₃ -4	Piperidine	Boiling C ₂ H ₅ OH	 (72)	197
D. Aromatic Aldehydes				
Benzaldehyde	(C ₂ H ₅) ₂ NH	Room	C ₆ H ₅ CH[CH(CO ₂ C ₂ H ₅)COCH ₂ CO ₂ C ₂ H ₅] ₂ (Quant.)	178
Salicylaldehyde	Piperidine	Water bath	 (78)	195
"	"	Water bath	 (87)†	195
Phthalaldehyde	(C ₂ H ₅) ₂ NH	Water bath	 (48)	193

6-Hydroxyfulvene-3,4-dicarboxaldehyde	$(C_2H_5)_3N$	Boiling $CHCl_3$	 (41)	710
2-Hydroxy-3-methoxybenzaldehyde (orthovanillin)	Piperidine	Boiling C_2H_5OH	 (33)	146
3,4-Methylenedioxyphthalaldehyde	Piperidine/dioxane	Water bath	 (47)	1151
6-Dimethylaminofulvene-3,4-dicarboxaldehyde	$(C_2H_5)_3N$	Boiling C_2H_5OH	 (75)	710
2-Hydroxy-1-naphthaldehyde	Piperidine	Water bath	 (53)	195
2-Aminoazulene-1-carboxaldehyde	„	„	 (—)	717, 718
6-Methylphenylaminofulvene-3,4-dicarboxaldehyde	$(C_2H_5)_3N + Al_2O_3$	Boiling $CHCl_3$	 (40)	710

Note: References 285 to 1153 are on pp. 582-599.

† Salicylaldehyde in 100% excess was used.




TABLE XII—Continued
CONDENSATIONS WITH DIETHYL ACETONEDICARBOXYLATE

D. Aromatic Aldehydes—Continued				
Aldehyde	Catalyst	Temperature	Product(s) and Yield(s) (%)	Refs.
6-Methylphenylaminofulvene-3,4-dicarboxaldehyde (contd.)	$(C_2H_5)_3N$	Boiling $CHCl_3$	 (50)	710
	Piperidinium acetate	„	 (—)	710
E. Heterocyclic Aldehydes				
4,5-Dichlorothiophene-2-carboxaldehyde	Piperidine	-5°	 (42)	578
Pyridine-2-carboxaldehyde	„	-10°	 (48)	982
	„	130°	 (49)	983

Note: References 285 to 1153 are on pp. 582-599.

§ The use of dimethyl acetonedicarboxylate gave 17% of the corresponding pyranone.



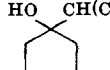
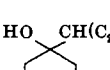
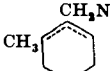
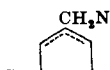
TABLE XIII
CONDENSATIONS WITH ALIPHATIC NITRO COMPOUNDS

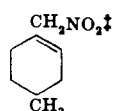
A. Acyclic Ketones					
Ketone	Nitro Compound	Catalyst	Temperature	Product(s) and Yield(s) (%)	Refs.
Acetone	CH ₃ NO ₂	Piperidine, pyridine, or CH ₃ NH ₂	Room	(CH ₃) ₂ C(CH ₂ NO ₂) ₂ (15-25, 68)	40, 207
	"	Piperidine	"	(CH ₃) ₂ C(CH ₂ NO ₂) ₂ (65)* + CH ₃ COCH ₂ C(CH ₃) ₂ CH ₂ NO ₂ (10)	208, 984
C ₂ H ₅ COCH ₃	CH ₃ NO ₂	Piperidine, pyridine, CH ₃ NH ₂ , or (C ₂ H ₅) ₂ NH	Room or reflux	C ₂ H ₅ (CH ₃)C(CH ₂ NO ₂) ₂ (15-30)	40, 208
	"	Piperidine	20°	C ₂ H ₅ C(CH ₃)=CHNO ₂ (Low) + C ₂ H ₅ C(CH ₃)CH ₂ NO ₂ (Low)	207
n-C ₃ H ₇ COCH ₃	CH ₃ NO ₂	Piperidine or (C ₂ H ₅) ₂ NH	Room or reflux	+ C ₂ H ₅ (CH ₃)C(CH ₂ NO ₂) ₂ (Low) n-C ₃ H ₇ (CH ₃)C(CH ₂ NO ₂) ₂ (15-30)	208
C ₂ H ₅ COC ₂ H ₅	"	"	"	(C ₂ H ₅) ₂ C=CHNO ₂ (Minor) + (C ₂ H ₅) ₂ C(CH ₂ NO ₂) ₂ (Major)	40, 208
i-C ₄ H ₉ COCH ₃	CH ₃ NO ₂	Piperidine	105°	i-C ₄ H ₉ (CH ₃)C(CH ₂ NO ₂) ₂ (15)	208
B. Alicyclic Ketones					
Cyclopentanone	CH ₃ NO ₂	Piperidine/C ₂ H ₅ OH	Room	 (Poor)	40
Cyclohexanone	CH ₃ NO ₂	"	"	 (30) +  (10)	40

Note: References 285 to 1153 are on pp. 582-599.

* The proportions in which the products were formed varied with catalysts and conditions.

TABLE XIII—Continued
CONDENSATIONS WITH ALIPHATIC NITRO COMPOUNDS

B. Alicyclic Ketones—Continued					
Ketone	Nitro Compound	Catalyst	Temperature	Product(s) and Yield(s) (%)	Refs.
Cyclohexanone (contd.)	CH ₃ NO ₂	(C ₂ H ₅) ₂ NH	B.p.	 (Small)	207
	"	Anhydrous liq. (CH ₃) ₂ NH	8-10°	 (48)	204
	C ₂ H ₅ NO ₂	Piperidine	Room	 (45)	40
	n-C ₃ H ₇ NO ₂	"	"	 (10)	40
2-Methylcyclohexanone	CH ₃ NO ₂	"	Reflux	 (8)	204
3-Methylcyclohexanone	CH ₃ NO ₂	"	"	 (30)	204



C. Aromatic Aldehydes

Aldehyde	Nitro Compound	Catalyst	Temperature	Product(s) and Yield(s) (%)	Refs.
2,4-Dichloro-benzaldehyde	$\text{C}_6\text{H}_3\text{NO}_2$ $n\text{-C}_4\text{H}_9\text{NO}_2$ $2\text{-ClC}_6\text{H}_4\text{CH}_2\text{NO}_2$ $4\text{-BrC}_6\text{H}_4\text{CH}_2\text{NO}_2$ $\text{C}_6\text{H}_5\text{CH}_2\text{NO}_2$	$n\text{-C}_4\text{H}_9\text{NH}_2$ $n\text{-C}_4\text{H}_9\text{NH}_2$ § § §	Boiling $\text{C}_2\text{H}_5\text{OH}$ 2° — — —	$2,4\text{-Cl}_2\text{C}_6\text{H}_3\text{CH}=\text{C}(\text{NO}_2)\text{CH}_3$ (73) $2,4\text{-Cl}_2\text{C}_6\text{H}_3\text{CH}=\text{C}(\text{NO}_2)\text{C}_6\text{H}_5$ (—) $2,4\text{-Cl}_2\text{C}_6\text{H}_3\text{CH}=\text{C}(\text{NO}_2)\text{C}_6\text{H}_4\text{Cl-2}$ (78) $2,4\text{-Cl}_2\text{C}_6\text{H}_3\text{CH}=\text{C}(\text{NO}_2)\text{C}_6\text{H}_4\text{Br-4}$ (—) $2,4\text{-Cl}_2\text{C}_6\text{H}_3\text{CH}=\text{C}(\text{NO}_2)\text{C}_6\text{H}_5$ (84) $2,6\text{-Cl}_2\text{C}_6\text{H}_3\text{CH}=\text{C}(\text{NO}_2)\text{C}_6\text{H}_5$ (83)	985 986 28, 987 987 28 28, 987
2,6-Dichloro-benzaldehyde	$\text{C}_6\text{H}_3\text{NO}_2$ $\text{C}_6\text{H}_5\text{CH}_2\text{NO}_2$ $\text{C}_6\text{H}_5\text{CH}_2\text{NO}_2$	$n\text{-C}_4\text{H}_9\text{NH}_2$ § §	Boiling $\text{C}_2\text{H}_5\text{OH}$ — —	$3,4\text{-Cl}_2\text{C}_6\text{H}_3\text{CH}=\text{C}(\text{NO}_2)\text{CH}_3$ (52) $3,4\text{-Cl}_2\text{C}_6\text{H}_3\text{CH}=\text{C}(\text{NO}_2)\text{C}_6\text{H}_5$ (65) $2,6\text{-Cl}_2\text{-3-HOC}_6\text{H}_3\text{CH}=\text{C}(\text{NO}_2)\text{C}_6\text{H}_5$ (91)	985 28, 987 28
3,4-Dichloro-benzaldehyde	$\text{C}_6\text{H}_3\text{NO}_2$ $\text{C}_6\text{H}_5\text{CH}_2\text{NO}_2$ $\text{C}_6\text{H}_5\text{CH}_2\text{NO}_2$	$n\text{-C}_4\text{H}_9\text{NH}_2$ § §	Boiling $\text{C}_2\text{H}_5\text{OH}$ — —	$3,4\text{-Cl}_2\text{C}_6\text{H}_3\text{CH}=\text{C}(\text{NO}_2)\text{CH}_3$ (52) $3,4\text{-Cl}_2\text{C}_6\text{H}_3\text{CH}=\text{C}(\text{NO}_2)\text{C}_6\text{H}_5$ (65) $2,6\text{-Cl}_2\text{-3-HOC}_6\text{H}_3\text{CH}=\text{C}(\text{NO}_2)\text{C}_6\text{H}_5$ (91)	985 28, 987 28
2,6-Dichloro-3-hydroxybenzaldehyde	$\text{C}_6\text{H}_5\text{CH}_2\text{NO}_2$ $\text{C}_6\text{H}_5\text{CH}_2\text{NO}_2$	§ §	— —	$2,6\text{-Cl}_2\text{-3-HOC}_6\text{H}_3\text{CH}=\text{C}(\text{NO}_2)\text{C}_6\text{H}_5$ (91)	28
2,4-Dinitro-benzaldehyde	CH_3NO_2	$(\text{C}_2\text{H}_5)_3\text{N}$	Room	$2,4\text{-(O}_2\text{N)}_2\text{C}_6\text{H}_3\text{CHOHCH}_2\text{NO}_2$ (41)	41
2-Fluoro-6-chloro-benzaldehyde	$2\text{-ClC}_6\text{H}_4\text{CH}_2\text{NO}_2$	§	—	$2\text{-F-6-ClC}_6\text{H}_3\text{CH}=\text{C}(\text{NO}_2)\text{C}_6\text{H}_4\text{Cl-2}$ (—)	987
2-BrC ₆ H ₄ CHO	CH_3NO_2	Piperidine + $n\text{-C}_4\text{H}_9\text{NH}_2$ or $(\text{CH}_3)_3\text{N}$	Room	$2\text{-BrC}_6\text{H}_4\text{CH}=\text{CHNO}_2$ (60)	211, 988
	$2\text{-ClC}_6\text{H}_4\text{CH}_2\text{NO}_2$ $4\text{-BrC}_6\text{H}_4\text{CH}_2\text{NO}_2$	§ §	— —	$2\text{-BrC}_6\text{H}_4\text{CH}=\text{C}(\text{NO}_2)\text{C}_6\text{H}_4\text{Cl-2}$ (—) $2\text{-BrC}_6\text{H}_4\text{CH}=\text{C}(\text{NO}_2)\text{C}_6\text{H}_4\text{Br-4}$ (—)	987 987

Note: References 285 to 1153 are on pp. 582-599.

† The position of the double bond was not established.

‡ Almost half of the ketone was recovered.

§ The Schiff base from RCHO and *n*-butylamine was treated with acetic acid and the nitro compound.

TABLE XIII—Continued
CONDENSATIONS WITH ALIPHATIC NITRO COMPOUNDS

C. Aromatic Aldehydes—Continued

Aldehyde	Nitro Compound	Catalyst	Temperature	Product(s) and Yield(s) (%)	Refs.
2-BrC ₆ H ₄ CHO (contd.)	$\text{C}_6\text{H}_5\text{CH}_2\text{NO}_2$	$\text{CH}_3\text{NH}_2\text{Cl}$ + Na_2CO_3	Boiling $\text{C}_2\text{H}_5\text{OH}$	"A diphenyl- <i>o</i> -bromophenylisoxazole"	211
	$\text{C}_6\text{H}_5\text{CH}_2\text{NO}_2$	§	—	$2\text{-BrC}_6\text{H}_4\text{CH}=\text{C}(\text{NO}_2)\text{C}_6\text{H}_5$ (85)	28, 987
3-BrC ₆ H ₄ CHO	$\text{C}_6\text{H}_5\text{CH}_2\text{NO}_2$	§	—	$3\text{-BrC}_6\text{H}_4\text{CH}=\text{C}(\text{NO}_2)\text{C}_6\text{H}_5$ (—)	987
4-BrC ₆ H ₄ CHO	CH_3NO_2	$n\text{-C}_4\text{H}_9\text{NH}_2$	100°	$4\text{-BrC}_6\text{H}_4\text{CH}=\text{CHNO}_2$ (67)	27
	$\text{CH}_3\text{CO}_2\text{NH}_4$	$n\text{-C}_4\text{H}_9\text{NH}_2$	Boiling $\text{CH}_3\text{CO}_2\text{H}$	$4\text{-BrC}_6\text{H}_4\text{CH}=\text{CHNO}_2$ (56)	989
	$2\text{-ClC}_6\text{H}_4\text{CH}_2\text{NO}_2$	§	—	$4\text{-BrC}_6\text{H}_4\text{CH}=\text{C}(\text{NO}_2)\text{C}_6\text{H}_4\text{Cl-2}$ (—)	987
	$\text{C}_6\text{H}_5\text{CH}_2\text{NO}_2$	$\text{CH}_3\text{NH}_2\text{Cl}$ + Na_2CO_3	Boiling $\text{C}_2\text{H}_5\text{OH}$	"A diphenyl <i>p</i> -bromophenylisoxazole" (—)	211
	$\text{C}_6\text{H}_5\text{CH}_2\text{NO}_2$	§	—	$4\text{-BrC}_6\text{H}_4\text{CH}=\text{C}(\text{NO}_2)\text{C}_6\text{H}_5$ (—)	987
2-ClC ₆ H ₄ CHO	$\text{C}_6\text{H}_5\text{NO}_2$	$n\text{-C}_4\text{H}_9\text{NH}_2$	Boiling $\text{C}_2\text{H}_5\text{OH}$	$2\text{-ClC}_6\text{H}_4\text{CH}=\text{C}(\text{NO}_2)\text{CH}_3$ (52)	985
	$\text{C}_6\text{H}_5\text{O}_2\text{CCH}_2\text{NO}_2$	$(\text{C}_2\text{H}_5)_3\text{N}$	20°	$2\text{-ClC}_6\text{H}_4\text{CH}[\text{CH}(\text{NO}_2)\text{CO}_2\text{C}_2\text{H}_5]_2$ (88)	990
	$2\text{-ClC}_6\text{H}_4\text{CH}_2\text{NO}_2$	§	—	$2\text{-ClC}_6\text{H}_4\text{CH}=\text{C}(\text{NO}_2)\text{C}_6\text{H}_4\text{Cl-2}$ (63)	28, 987
	$2\text{-FC}_6\text{H}_4\text{CH}_2\text{NO}_2$	§	—	$2\text{-ClC}_6\text{H}_4\text{CH}=\text{C}(\text{NO}_2)\text{C}_6\text{H}_4\text{F-2}$ (68)	28, 987
	$\text{C}_6\text{H}_5\text{CH}_2\text{NO}_2$		—	$2\text{-ClC}_6\text{H}_4\text{CH}=\text{C}(\text{NO}_2)\text{C}_6\text{H}_5$ (87)	28, 987
4-ClC ₆ H ₄ CHO	$\text{C}_6\text{H}_5\text{O}_2\text{CCH}_2\text{NO}_2$	$(\text{C}_2\text{H}_5)_3\text{N}$	20°	$4\text{-ClC}_6\text{H}_4\text{CH}[\text{CH}(\text{NO}_2)\text{CO}_2\text{C}_2\text{H}_5]_2$ (62)	990
	$n\text{-C}_4\text{H}_9\text{NO}_2$	$n\text{-C}_4\text{H}_9\text{NH}_2$	2°	$4\text{-ClC}_6\text{H}_4\text{CH}=\text{C}(\text{NO}_2)\text{C}_6\text{H}_5$ (—)	986
	$n\text{-C}_4\text{H}_9\text{NO}_2$	$n\text{-C}_4\text{H}_9\text{NH}_2$	Boiling C_6H_6	$4\text{-ClC}_6\text{H}_4\text{CH}=\text{C}(\text{NO}_2)\text{C}_6\text{H}_7\text{-n}$ (—)	991
	$\text{C}_6\text{H}_5\text{CH}_2\text{NO}_2$	§	—	$4\text{-ClC}_6\text{H}_4\text{CH}=\text{C}(\text{NO}_2)\text{C}_6\text{H}_5$ (75)	28, 987
	$\text{C}_6\text{H}_5\text{CH}_2\text{NO}_2$	$n\text{-C}_4\text{H}_9\text{NH}_2$	2°	$4\text{-ClC}_6\text{H}_4\text{CH}=\text{C}(\text{NO}_2)\text{C}_6\text{H}_5$ (—)	986
2-Cl-3-HOC ₆ H ₃ CHO	CH_3NO_2	$\text{CH}_3\text{CO}_2\text{NH}_4$	Boiling $\text{CH}_3\text{CO}_2\text{H}$	$2\text{-Cl-3-HOC}_6\text{H}_3\text{CH}=\text{CHNO}_2$ (70)	992
2-FC ₆ H ₄ CHO	CH_3NO_2	$(\text{C}_2\text{H}_5)_3\text{N}$	Room	$2\text{-FC}_6\text{H}_4\text{CH}=\text{CHNO}_2$ (60)	993
	$2\text{-ClC}_6\text{H}_4\text{CH}_2\text{NO}_2$	§	—	$2\text{-FC}_6\text{H}_4\text{CH}=\text{C}(\text{NO}_2)\text{C}_6\text{H}_4\text{Cl-2}$ (—)	987
	$\text{C}_6\text{H}_5\text{CH}_2\text{NO}_2$	§	—	$2\text{-FC}_6\text{H}_4\text{CH}=\text{C}(\text{NO}_2)\text{C}_6\text{H}_5$ (52)	28, 987
4-FC ₆ H ₄ CHO	$\text{C}_6\text{H}_5\text{CH}_2\text{NO}_2$	§	—	$4\text{-FC}_6\text{H}_4\text{CH}=\text{C}(\text{NO}_2)\text{C}_6\text{H}_5$ (—)	987
4-IC ₆ H ₄ CHO	CH_3NO_2	$\text{CH}_3\text{CO}_2\text{NH}_4$	Boiling $\text{CH}_3\text{CO}_2\text{H}$	$4\text{-IC}_6\text{H}_4\text{CH}=\text{CHNO}_2$ (75)	989
	$\text{C}_6\text{H}_5\text{CH}_2\text{NO}_2$	§	—	$4\text{-IC}_6\text{H}_4\text{CH}=\text{C}(\text{NO}_2)\text{C}_6\text{H}_5$ (—)	987
2-O ₂ NC ₆ H ₄ CHO	CH_3NO_2	$(\text{C}_2\text{H}_5)_3\text{N}$	Room	$2\text{-O}_2\text{NC}_6\text{H}_4\text{CHOHCH}_2\text{NO}_2$ (75)	41
	$\text{C}_6\text{H}_5\text{NO}_2$	$n\text{-C}_4\text{H}_9\text{NH}_2$	Boiling $\text{C}_2\text{H}_5\text{OH}$	$2\text{-O}_2\text{NC}_6\text{H}_4\text{CH}=\text{C}(\text{NO}_2)\text{CH}_3$ (46)	985
	$\text{C}_6\text{H}_5\text{O}_2\text{CCH}_2\text{NO}_2$	$(\text{C}_2\text{H}_5)_3\text{N}$	20°	$2\text{-O}_2\text{NC}_6\text{H}_4\text{CH}[\text{CH}(\text{NO}_2)\text{CO}_2\text{C}_2\text{H}_5]_2$ (68)	990

3-O ₂ NC ₆ H ₄ CHO	2-ClC ₆ H ₄ CH ₂ NO ₂	§	—	2-O ₂ NC ₆ H ₄ CH=C(NO ₂)C ₆ H ₄ Cl-2 (81)	28, 987
	C ₆ H ₅ CH ₂ NO ₂	§	—	2-O ₂ NC ₆ H ₄ CH=C(NO ₂)C ₆ H ₅ (45)	28
	CH ₃ NO ₂	CH ₃ NH ₂ Cl + Na ₂ CO ₃ ; Room or (C ₂ H ₅) ₃ N		3-O ₂ NC ₆ H ₄ CH=CHNO ₂ (30, 47)	27, 372
4-O ₂ NC ₆ H ₄ CHO	C ₆ H ₅ NO ₂	n-C ₆ H ₁₁ NH ₂	2°	3-O ₂ NC ₆ H ₄ CH=C(NO ₂)CH ₃ (—)	986
	C ₆ H ₅ O ₂ CCH ₂ NO ₂	(C ₂ H ₅) ₂ NH	20°	3-O ₂ NC ₆ H ₄ CH[CH(NO ₂)CO ₂ C ₂ H ₅] ₂ (66)	990
	C ₆ H ₅ NO ₂	n-C ₆ H ₁₁ NH ₂	Boiling C ₂ H ₅ OH	4-O ₂ NC ₆ H ₄ CH=C(NO ₂)CH ₃ (55)	985
	n-C ₆ H ₇ NO ₂	n-C ₆ H ₁₁ NH ₂	2°	4-O ₂ NC ₆ H ₄ CH=C(NO ₂)C ₆ H ₅ (—)	986
	C ₆ H ₅ O ₂ CCH ₂ NO ₂	(C ₂ H ₅) ₂ NH	20°	4-O ₂ NC ₆ H ₄ CH[CH(NO ₂)CO ₂ C ₂ H ₅] ₂ (60)	990
	C ₆ H ₅ CH ₂ NO ₂	CH ₃ NH ₂ or n-C ₆ H ₁₁ NH ₂	Steam bath or room	4-O ₂ NC ₆ H ₄ CH=C(NO ₂)C ₆ H ₅ (50)	994, 995
Benzaldehyde	CH ₃ NO ₂	§	—	4-O ₂ NC ₆ H ₄ CH=C(NO ₂)C ₆ H ₅ (65)	28
	"	n-C ₆ H ₁₁ NH ₂	Room	C ₆ H ₅ CH=CHNO ₂ (75)	199
	"	¶	100°	C ₆ H ₅ CH=CHNO ₂ (0-77)	27
	"	CH ₃ CO ₂ NH ₄	Boiling CH ₃ CO ₂ H	C ₆ H ₅ CH=CHNO ₂ (60)	254
	"	**	Boiling C ₂ H ₅ OH	C ₆ H ₅ CH(NHC ₆ H ₅)CH ₂ NO ₂ (—)	200
	BrCH ₂ NO ₂	n-C ₆ H ₁₁ NH ₂	100°	C ₆ H ₅ CH=C(Br)NO ₂ (25)	27
	C ₆ H ₅ NO ₂	C ₆ H ₅ NH ₂ or n-C ₆ H ₁₁ NH ₂	Room	C ₆ H ₅ CH=C(NO ₂)CH ₃ (76)	199
	"	**	Boiling CH ₃ OH	C ₆ H ₅ CH(NHC ₆ H ₅)CH(NO ₂)CH ₃ (30)	200
	"	n-C ₆ H ₉ NH ₂	Boiling C ₂ H ₅ OH	C ₆ H ₅ CH=C(NO ₂)CH ₃ (85)	996
	"	CH ₃ CO ₂ NH ₄	Boiling CH ₃ CO ₂ H	C ₆ H ₅ CH=C(NO ₂)CH ₃ (55)	254
	"	n-C ₆ H ₉ NH ₂	Boiling xylene	C ₆ H ₅ CH=C(NO ₂)CH ₃ (85)	997
	"	H ₂ NCH ₂ CH ₂ NH ₂	50°	C ₆ H ₅ CH=C(NO ₂)CH ₃ (76)	998
	n-C ₆ H ₇ NO ₂	n-C ₆ H ₉ NH ₂	Boiling C ₂ H ₅ OH	C ₆ H ₅ CH=C(NO ₂)C ₆ H ₅ (—)	996
	n-C ₆ H ₉ NO ₂	"	"	C ₆ H ₅ CH=C(NO ₂)C ₆ H _{7-n} (—)	996
	C ₆ H ₅ O ₂ CCH ₂ NO ₂	CH ₃ NH ₂ /C ₂ H ₅ OH	20°	C ₆ H ₅ CH[CH(NO ₂)CO ₂ C ₂ H ₅] ₂ (Good)	990
	4-ClC ₆ H ₄ CH ₂ NO ₂	§	—	C ₆ H ₅ CH=C(NO ₂)C ₆ H ₄ Cl-4 (54)	28, 987
	4-CH ₃ OC ₆ H ₄ CH ₂ NO ₂	CH ₃ NH ₂ Cl + Na ₂ CO ₃	Room	C ₆ H ₅ CH=C(NO ₂)C ₆ H ₄ OCH ₃ -4 (45)	930
	C ₆ H ₅ CH ₂ NO ₂	CH ₃ NH ₂ Cl + Na ₂ CO ₃ ; or n-C ₆ H ₁₁ NH ₂	"	C ₆ H ₅ CH=C(NO ₂)C ₆ H ₅ (65)	199, 995

Note: References 285 to 1153 are on pp. 582-599.

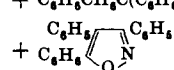
§ The Schiff base from RCHO and *n*-butylamine was treated with acetic acid and the nitro compound.

¶ The Schiff base from RCHO and *n*-propylamine was treated with acetic acid and the nitro compound.

¶ Eighteen catalysts (primary, secondary, and tertiary amines) were used.

** The Schiff base from RCHO and aniline was used.

TABLE XIII—Continued
CONDENSATIONS WITH ALIPHATIC NITRO COMPOUNDS

C. Aromatic Aldehydes—Continued					
Aldehyde	Nitro Compound	Catalyst	Temperature	Product(s) and Yield(s) (%)	Refs.
Benzaldehyde (contd.)	C ₆ H ₅ CH ₂ NO ₂	Aliphatic amines	Room	C ₆ H ₅ CH=C(NO ₂)C ₆ H ₅ (50) (<i>cis</i> and <i>trans</i>) + C ₆ H ₅ CH[CH(NO ₂)C ₆ H ₅] ₂ + C ₆ H ₅ CH ₂ C(C ₆ H ₅)=C(NO ₂)C ₆ H ₅ 	64
	"	Piperidine + n-C ₆ H ₁₁ CO ₂ H	Boiling C ₆ H ₆	C ₆ H ₅ CH=C(NO ₂)C ₆ H ₅ (68)	69
Salicylaldehyde 4-Hydroxy- benzaldehyde	"	§	—	C ₆ H ₅ CH=C(NO ₂)C ₆ H ₅ (88)	28
	C ₆ H ₅ O ₂ CCH ₂ NO ₂	(C ₂ H ₅) ₂ NH	20°	2-HOC ₆ H ₄ CH[CH(NO ₂)CO ₂ C ₂ H ₅] ₂ (98)	990
	CH ₃ NO ₂	C ₆ H ₅ NH ₂	Water bath	4-HOC ₆ H ₄ CH=CHNO ₂ (79)	985
	"	CH ₃ CO ₂ NH ₄	Boiling CH ₃ CO ₂ H	4-HOC ₆ H ₄ CH=CHNO ₂ (60)	254
	C ₆ H ₅ NO ₂	n-C ₆ H ₁₁ NH ₂	Boiling C ₂ H ₅ OH	4-HOC ₆ H ₄ CH=C(NO ₂)CH ₃ (29)	985
	"	CH ₃ CO ₂ NH ₄	Boiling CH ₃ CO ₂ H	4-HOC ₆ H ₄ CH=C(NO ₂)CH ₃ (35)	254
4-Sulfamyl- benzaldehyde	C ₆ H ₅ O ₂ CCH ₂ NO ₂	(C ₂ H ₅) ₂ NH	20°	††	990
	C ₆ H ₅ CH ₂ NO ₂	§	—	4-HOC ₆ H ₄ CH=C(NO ₂)C ₆ H ₅ (33)	28
	CH ₃ NO ₂	n-C ₆ H ₁₁ NH ₂	2°	4-H ₂ NO ₂ SC ₆ H ₄ CH=CHNO ₂ (—)	986
	"	"	"	"	"
5-Bromopiperonal Isophthalaldehyde Terephthalaldehyde	C ₆ H ₅ NO ₂	n-C ₆ H ₉ NH ₂	Boiling C ₆ H ₆	4-H ₂ NO ₂ SC ₆ H ₄ CH=C(NO ₂)CH ₃ (—)	991
	CH ₂ NO ₂	CH ₃ CO ₂ NH ₄	Boiling CH ₃ CO ₂ H	3,4-CH ₃ O ₂ C ₆ H ₃ CH=CHNO ₂ (37)	999
	C ₆ H ₅ NO ₂	n-C ₆ H ₁₁ NH ₂	37°	C ₆ H ₄ [CH=C(NO ₂)CH ₃] ₂ -1,3 (67)	985
	C ₆ H ₅ NO ₂	(C ₂ H ₅) ₂ N	Water bath	C ₆ H ₄ [CH=C(NO ₂)CH ₃] ₂ -1,4 (Poor)	215
3,4-Methylenedioxy- benzaldehyde (piperonal)	"	H ₂ NCH ₂ CH ₂ NH ₂	Room	C ₆ H ₄ [CH=C(NO ₂)CH ₃] ₂ -1,4 (47)	697
	C ₆ H ₅ CH ₂ NO ₂	n-C ₆ H ₁₁ NH ₂	Water bath	C ₆ H ₄ [CH=C(NO ₂)C ₆ H ₅] ₂ -1,4 (60)	215
	"	H ₂ NCH ₂ CH ₂ NH ₂	Room	C ₆ H ₄ [CH=C(NO ₂)C ₆ H ₅] ₂ -1,4 (46)	697
	CH ₃ NO ₂	CH ₃ NH ₂ Cl + Na ₂ CO ₃	"	3,4-CH ₃ O ₂ C ₆ H ₃ CH=CHNO ₂ (93)	199
	"	n-C ₆ H ₁₁ NH ₂	100°	3,4-CH ₃ O ₂ C ₆ H ₃ CH=CHNO ₂ (96)	27
	"	C ₆ H ₅ NH ₂ or H ₂ NCH ₂ CH ₂ NH ₂	8-10°	3,4-CH ₃ O ₂ C ₆ H ₃ CH=CHNO ₂ (97)	998, 1000

	$C_4H_5NO_2$	$(C_2H_5)_3N/C_2H_5OH$ $C_2H_5NH_2$, or $n-C_4H_9NH_2$, or CH_3NH_2Cl + Na_2CO_3	Room, then 0° Room	$3,4-CH_2O_2C_6H_3CH(OCOCH_3)CH_2NO_2$ †† (33) $3,4-CH_2O_2C_6H_3CH=C(NO_2)CH_3$ (87)	1001 199, 1002, 1003
	$C_6H_5CH_2NO_2$	CH_3NH_2Cl + Na_2CO_3 ; or $C_2H_5NH_2$	Room	$3,4-CH_2O_2C_6H_3CH=C(NO_2)C_6H_5$ (82)	199
	"	§	—	$3,4-CH_2O_2C_6H_3CH=C(NO_2)C_6H_5$ (63) $3,5-Br_2-2-CH_2OC_6H_2CH=C(NO_2)C_6H_5$ (—)	28 987
3,5-Dibromo-2-methoxybenzaldehyde	$C_6H_5CH_2NO_2$	§	—		
2,3-Dibromo-4-hydroxy-5-methoxybenzaldehyde	CH_3NO_2	$CH_3CO_2NH_4$	Boiling CH_3CO_2H	$2,3-Br_2-4-HO-5-CH_3OC_6H_2CH=CHNO_2$ (52)	1004
5-Bromo-2-nitro-4-hydroxy-3-methoxybenzaldehyde	CH_3NO_2	"	"	$5-Br-2-O_2N-4-HO-3-CH_3OC_6H_2CH=CHNO_2$ (82)	1004
2,6-Dichloro-3-methoxybenzaldehyde	CH_3NO_2	"	"	$2,6-Cl_2-3-CH_3OC_6H_2CH=CHNO_2$ (70)	992
2-Bromo-4-hydroxy-3-methoxybenzaldehyde	CH_3NO_2	"	"	$2-Br-4-HO-3-CH_3OC_6H_2CH=CHNO_2$ (67)	1004
2-Bromo-4-hydroxy-5-methoxybenzaldehyde	CH_3NO_2	"	"	$2-Br-4-HO-5-CH_3OC_6H_2CH=CHNO_2$ (64)	1004
3-Bromo-4-hydroxy-5-methoxybenzaldehyde	CH_3NO_2	"	"	$3-Br-4-HO-5-CH_3OC_6H_2CH=CHNO_2$ (50)	1004
2-Chloro-3-methoxybenzaldehyde	CH_3NO_2	"	"	$2-Cl-3-CH_3OC_6H_3CH=CHNO_2$ (80)	992
2-Iodo-3-methoxybenzaldehyde	CH_3NO_2	"	"	$2-I-3-CH_3OC_6H_3CH=CHNO_2$ (75)	992
3-Iodo-4-hydroxy-5-methoxybenzaldehyde	CH_3NO_2	"	"	$3-I-4-HO-5-CH_3OC_6H_2CH=CHNO_2$ (—)	464

Note: References 285 to 1153 are on pp. 582-599.

§ The Schiff base from RCHO and *n*-butylamine was treated with acetic acid and the nitro compound.

†† The usual product was converted without isolation to $4-HOC_6H_4CON(C_2H_5)_2$
 $C_2H_5O_2C \rightarrow O$

‡‡ The crude product was acetylated.

TABLE XIII—Continued
CONDENSATIONS WITH ALIPHATIC NITRO COMPOUNDS

C. Aromatic Aldehydes—Continued					
Aldehyde	Nitro Compound	Catalyst	Temperature	Product(s) and Yield(s) (%)	Refs.
2-Nitro-4-methylbenzaldehyde	CH_3NO_2	$CH_3CO_2NH_4$	Boiling CH_3CO_2H	$2-O_2N-4-CH_3C_6H_3CH=CHNO_2$ (65)	992
2-Nitro-3-methoxybenzaldehyde	CH_3NO_2	"	"	$2-O_2N-3-CH_3OC_6H_3CH=CHNO_2$ (85)	992
2-Nitro-4-methoxybenzaldehyde	CH_3NO_2	"	"	$2-O_2N-4-CH_3OC_6H_3CH=CHNO_2$ (70)	992
2-Nitro-5-methoxybenzaldehyde	CH_3NO_2	"	"	$2-O_2N-5-CH_3OC_6H_3CH=CHNO_2$ (80)	992
2-Nitro-4-hydroxy-3-methoxybenzaldehyde	CH_3NO_2	"	"	$2-O_2N-4-HO-3-CH_3OC_6H_2CH=CHNO_2$ (65)	1004
3-Nitro-4-hydroxy-5-methoxybenzaldehyde	CH_3NO_2 $C_2H_5NO_2$	" CH_3NH_2Cl + Na_2CO_3	Room	$3-O_2N-4-HO-5-CH_3OC_6H_2CH=CHNO_2$ (73) $3-O_2N-4-HO-5-CH_3OC_6H_2CH=C(NO_2)CH_3$ (55)	1004, 464 1002
2- $CH_3C_6H_4CHO$	$C_2H_5NO_2$ $C_6H_5CH_2NO_2$	$CH_3CO_2NH_4$ §	Boiling CH_3CO_2H Room	$2-CH_3C_6H_4CH=C(NO_2)CH_3$ (55) $2-CH_3C_6H_4CH=C(NO_2)C_6H_5$ (56)	427 28
4- $CH_3C_6H_4CHO$	CH_3NO_2 " $C_2H_5NO_2$ " $C_6H_5CH_2NO_2$ " $n-C_4H_9NO_2$ " $C_6H_5CH_2NO_2$	$n-C_4H_9NH_2$ $H_2NCH_2CH_2NH_2$ $n-C_4H_9NH_2$ $H_2NCH_2CH_2NH_2$ $n-C_4H_9NH_2$ "	Steam bath 8-10° Steam bath 80° Boiling C_6H_6 Room	$4-CH_3C_6H_4CH=CHNO_2$ (60) $4-CH_3C_6H_4CH=CHNO_2$ (96) $4-CH_3C_6H_4CH=C(NO_2)CH_3$ (50) $4-CH_3C_6H_4CH=C(NO_2)CH_3$ (86) $4-CH_3C_6H_4CH=C(NO_2)C_3H_7-n$ (—) $4-CH_3C_6H_4CH=C(NO_2)C_6H_5$ (66)	1005 998 986, 1005 998 991 995
	"	§	—	$4-CH_3C_6H_4CH=C(NO_2)C_6H_5$ (84)	28
2-Methoxybenzaldehyde	CH_3NO_2 " $n-C_3H_7NO_2$ " $2-ClC_6H_4CH_2NO_2$ $C_2H_5NO_2$ "	$(C_2H_5)_3N$ $CH_3CO_2NH_4$ " $n-C_4H_9NH_2$ § § "	Steam bath Boiling CH_3CO_2H " CH_3CO_2H — — Boiling C_2H_5OH Boiling CH_3CO_2H	$2-CH_3OC_6H_4CH=CHNO_2$ (—) $2-CH_3OC_6H_4CH=CHNO_2$ (82) $2-CH_3OC_6H_4CH=C(NO_2)C_2H_5$ (34) $2-CH_3OC_6H_4CH=C(NO_2)C_6H_5$ (74) $2-CH_3OC_6H_4CH=C(NO_2)C_6H_4Cl-2$ (74) $3-CH_3OC_6H_4CH=C(NO_2)CH_3$ (54) $3-CH_3OC_6H_4CH=C(NO_2)CH_3$ (65)	1006 254 254 28 28, 987 985 1007

4-Methoxy-benzaldehyde (anisaldehyde)	CH ₃ NO ₂	CH ₃ NH ₂ Cl + Na ₂ CO ₃	Room	4-CH ₃ OC ₆ H ₄ CH=CHNO ₂ (86)	199
"	"	n-C ₄ H ₉ NH ₂	100°	4-CH ₃ OC ₆ H ₄ CH=CHNO ₂ (62)	27
"	"	H ₂ NCH ₂ CH ₂ NH ₂	8-10°	4-CH ₃ OC ₆ H ₄ CH=CHNO ₂ (97)	998
"	"	CH ₃ CO ₂ NH ₄	Boiling CH ₃ CO ₂ H	4-CH ₃ OC ₆ H ₄ CH=CHNO ₂ (65)	254
"	C ₂ H ₅ NO ₂	n-C ₄ H ₉ NH ₂	Room	4-CH ₃ OC ₆ H ₄ CH=C(NO ₂)CH ₃ (60)	199
"	"	C ₂ H ₅ NH ₂	80°	4-CH ₃ OC ₆ H ₄ CH=C(NO ₂)CH ₃ (100)	998
"	"	H ₂ NCH ₂ CH ₂ NH ₂	Boiling CH ₃ CO ₂ H	4-CH ₃ OC ₆ H ₄ CH=C(NO ₂)CH ₃ (80)	254
"	"	CH ₃ CO ₂ NH ₄	Boiling C ₂ H ₅ OH	4-CH ₃ OC ₆ H ₄ CH=C(NO ₂)C ₂ H ₅ (90)	996
n-C ₃ H ₇ NO ₂	"	n-C ₄ H ₉ NH ₂	"	4-CH ₃ OC ₆ H ₄ CH=C(NO ₂)C ₂ H ₅ -n (90)	996
n-C ₄ H ₉ NO ₂	"	"	"	4-CH ₃ OC ₆ H ₄ CH=C(NO ₂)C ₂ H ₅ -n (89)	990
C ₂ H ₅ O ₂ CCH ₂ NO ₂	"	(C ₂ H ₅) ₂ NH	20°	4-CH ₃ OC ₆ H ₄ CH=C(NO ₂)C ₂ H ₅ -4 (55)	930
4-CH ₃ OC ₆ H ₄ -CH ₂ NO ₂	"	CH ₃ NH ₂ Cl + Na ₂ CO ₃	Room	4-CH ₃ OC ₆ H ₄ CH=C(NO ₂)C ₆ H ₅ (85)	199
C ₆ H ₅ CH ₂ NO ₂	"	CH ₃ NH ₂ Cl + Na ₂ CO ₃ or (C ₂ H ₅) ₂ NH	"	4-CH ₃ OC ₆ H ₄ CH=C(NO ₂)C ₆ H ₅ (74)	28
2-Hydroxy-3-methoxy-benzaldehyde	CH ₃ NO ₂	CH ₃ CO ₂ NH ₄	Boiling CH ₃ CO ₂ H	2-HO-3-CH ₃ OC ₆ H ₄ CH=CHNO ₂ (75)	254, 1008
"	"	CH ₃ NH ₂	Room	2-HO-3-CH ₃ OC ₆ H ₄ CH=CHNO ₂ (45)	254
"	C ₂ H ₅ NO ₂	n-C ₄ H ₉ NH ₂	Boiling C ₂ H ₅ OH	2-HO-3-CH ₃ OC ₆ H ₄ CH=C(NO ₂)CH ₃ (27)	985
2-Hydroxy-4-methoxy-benzaldehyde	CH ₃ NO ₂	CH ₃ CO ₂ NH ₄ /alcohol	Boiling CH ₃ CO ₂ H	2-HO-3-CH ₃ OC ₆ H ₄ CH=C(NO ₂)CH ₃ (45)	254
3-Hydroxy-4-methoxy-benzaldehyde	CH ₃ NO ₂	CH ₃ CO ₂ NH ₄ /alcohol	Room	2-HO-4-CH ₃ OC ₆ H ₄ CH=CHNO ₂ (80)	1009
3-Methoxy-4-hydroxy-benzaldehyde (vanillin)	CH ₃ NO ₂	CH ₃ NH ₂ Cl + Na ₂ CO ₃	Room or 0°	3-HO-4-CH ₃ OC ₆ H ₄ CH=CHNO ₂ (80)	1008, 1010
"	"	"	Room	4-HO-3-CH ₃ OC ₆ H ₄ CH=CHNO ₂ (81)	199, 1008, 1011
"	"	n-C ₄ H ₉ NH ₂	100°	4-HO-3-CH ₃ OC ₆ H ₄ CH=CHNO ₂ (80)	27
"	"	CH ₃ NH ₂ or H ₂ NCH ₂ CH ₂ NH ₂	Room	4-HO-3-CH ₃ OC ₆ H ₄ CH=CHNO ₂ (95)	254, 998
"	"	(C ₂ H ₅) ₂ N/C ₂ H ₅ OH	"	4-CH ₃ CO ₂ -3-CH ₃ OC ₆ H ₄ CH(OCOCH ₃)CH ₂ NO ₂ †† (20)	1001
"	"	CH ₃ CO ₂ NH ₄	Boiling CH ₃ CO ₂ H	4-HO-3-CH ₃ OC ₆ H ₄ CH=CHNO ₂ (50)	254

Note: References 285 to 1153 are on pp. 582-599.

† The Schiff base from RCHO and n-butylamine was treated with acetic acid and the nitro compound.

†† The crude product was acetylated.

TABLE XIII—Continued
CONDENSATIONS WITH ALIPHATIC NITRO COMPOUNDS

C. Aromatic Aldehydes—Continued					
Aldehyde	Nitro Compound	Catalyst	Temperature	Product(s) and Yield(s) (%)	Refs.
3-Methoxy-4-hydroxy-benzaldehyde (vanillin) (contd.)	C ₂ H ₅ NO ₂	CH ₃ NH ₂ Cl + Na ₂ CO ₃	Room	4-HO-3-CH ₃ OC ₆ H ₄ CH=C(NO ₂)CH ₃ (79)	1002
"	"	CH ₃ CO ₂ NH ₄	Boiling CH ₃ CO ₂ H	4-HO-3-CH ₃ OC ₆ H ₄ CH=C(NO ₂)CH ₃ (20)	254
"	n-C ₄ H ₉ NO ₂	"	"	4-HO-3-CH ₃ OC ₆ H ₄ CH=C(NO ₂)C ₂ H ₅ (40)	254
"	C ₂ H ₅ CH ₂ NO ₂	§	—	4-HO-3-CH ₃ OC ₆ H ₄ CH=C(NO ₂)C ₂ H ₅ (24)	28
2-Methoxy-3,4-methylenedioxy-benzaldehyde	CH ₃ NO ₂	CH ₃ CO ₂ NH ₄	Boiling CH ₃ CO ₂ H	2-CH ₃ O-3,4-CH ₂ O ₂ C ₆ H ₃ CH=CHNO ₂ (80)	1012
3-Methoxy-4,5-methylenedioxy-benzaldehyde	CH ₃ NO ₂	n-C ₄ H ₉ NH ₂	Room	3-CH ₃ O-4,5-CH ₂ O ₂ C ₆ H ₃ CH=CHNO ₂ (90)	1013
2-Bromo-3,4-dimethoxy-benzaldehyde	CH ₃ NO ₂	CH ₃ CO ₂ NH ₄	Boiling CH ₃ CO ₂ H	2-Br-3,4-(CH ₃ O) ₂ C ₆ H ₃ CH=CHNO ₂ (77)	1014
3-Bromo-4,5-dimethoxy-benzaldehyde	CH ₃ NO ₂	CH ₃ NH ₂ Cl + Na ₂ CO ₃	—	3-Br-4,5-(CH ₃ O) ₂ C ₆ H ₃ CH=CHNO ₂ (85)	1015
"	"	CH ₃ CO ₂ NH ₄	Boiling CH ₃ CO ₂ H	3-Br-4,5-(CH ₃ O) ₂ C ₆ H ₃ CH=CHNO ₂ (55)	1016
3-Bromo-5,6-dimethoxy-benzaldehyde	CH ₃ NO ₂	"	"	3-Br-5,6-(CH ₃ O) ₂ C ₆ H ₃ CH=CHNO ₂ (—)	1017
2-Chloro-3-ethoxy-benzaldehyde	CH ₃ NO ₂	"	"	2-Cl-3-C ₂ H ₅ OC ₆ H ₃ CH=CHNO ₂ (76)	992
4-Methoxy-3-chloromethyl-benzaldehyde	CH ₃ NO ₂ C ₂ H ₅ NO ₂	n-C ₄ H ₉ NH ₂	Boiling C ₆ H ₆	4-CH ₃ O-3-ClCH ₂ C ₆ H ₃ CH=CHNO ₂ (—)	991
"	"	"	"	4-CH ₃ O-3-ClCH ₂ C ₆ H ₃ CH=C(NO ₂)CH ₃ (—)	991
3-Iodo-4,5-dimethoxy-benzaldehyde	CH ₃ NO ₂	CH ₃ CO ₂ NH ₄	Boiling CH ₃ CO ₂ H	3-I-4,5-(CH ₃ O) ₂ C ₆ H ₃ CH=CHNO ₂ (60)	464
4-Acetamido-benzaldehyde	C ₂ H ₅ NO ₂	n-C ₄ H ₉ NH ₂	Boiling C ₂ H ₅ OH or C ₆ H ₆	4-CH ₃ CONHC ₆ H ₄ CH=C(NO ₂)CH ₃ (30)	985, 991
2-Nitro-3,4-dimethoxy-benzaldehyde	CH ₃ NO ₂	CH ₃ CO ₂ NH ₄	Boiling CH ₃ CO ₂ H	2-O ₂ N-3,4-(CH ₃ O) ₂ C ₆ H ₃ CH=CHNO ₂ (33)	1018

3-Nitro-4,5-dimethoxybenzaldehyde	CH ₃ NO ₂	CH ₃ NH ₂ Cl + Na ₂ CO ₃	Room	3-O ₂ N-4,5-(CH ₃ O) ₂ C ₆ H ₂ CH=CHNO ₂ (30)	372
3-Nitro-4,6-dimethoxybenzaldehyde	CH ₃ NO ₂	CH ₃ CO ₂ NH ₄ /alcohol	Room	3-O ₂ N-4,6-(CH ₃ O) ₂ C ₆ H ₂ CH=CHNO ₂ (80)	1009
2-Ethoxybenzaldehyde	CH ₃ NO ₂	CH ₃ NH ₂	"	2-C ₂ H ₅ OC ₆ H ₄ CH=CHNO ₂ (30)	254
"	"	CH ₃ CO ₂ NH ₄	Boiling CH ₃ CO ₂ H	2-C ₂ H ₅ OC ₆ H ₄ CH=CHNO ₂ (20)	254
"	C ₂ H ₅ NO ₂	n-C ₄ H ₉ NH ₂	Boiling C ₂ H ₅ OH	2-C ₂ H ₅ OC ₆ H ₄ CH=C(NO ₂)CH ₃ (73)	985
"	2-ClC ₆ H ₄ CH ₂ NO ₂	§	—	2-C ₂ H ₅ OC ₆ H ₄ CH=C(NO ₂)C ₆ H ₄ Cl-2 (77)	28, 987
"	C ₆ H ₅ CH ₂ NO ₂	§	—	2-C ₂ H ₅ OC ₆ H ₄ CH=C(NO ₂)C ₆ H ₅ (67)	28
4-Hydroxy-3-ethoxybenzaldehyde	CH ₃ NO ₂	CH ₃ CO ₂ NH ₄	Boiling CH ₃ CO ₂ H	4-HO-3-C ₂ H ₅ OC ₆ H ₃ CH=CHNO ₂ (78)	254
"	"	CH ₃ NH ₂ /CH ₃ OH	Room	4-HO-3-C ₂ H ₅ OC ₆ H ₃ CH=CHNO ₂ (75)	254
"	C ₂ H ₅ NO ₂	CH ₃ CO ₂ NH ₄	Boiling CH ₃ CO ₂ H	4-HO-3-C ₂ H ₅ OC ₆ H ₃ CH=C(NO ₂)CH ₃ (50)	254
2,3-Dimethoxybenzaldehyde	CH ₃ NO ₂	CH ₃ NH ₂ /CH ₃ OH	Room	2,3-(CH ₃ O) ₂ C ₆ H ₃ CH=CHNO ₂ (50)	254
"	"	CH ₃ CO ₂ NH ₄	Boiling CH ₃ CO ₂ H	2,3-(CH ₃ O) ₂ C ₆ H ₃ CH=CHNO ₂ (60)	254, 1019
"	C ₂ H ₅ NO ₂	"	"	2,3-(CH ₃ O) ₂ C ₆ H ₃ CH=C(NO ₂)CH ₃ (75)	254
"	"	CH ₃ NH ₂ /CH ₃ OH	Room	2,3-(CH ₃ O) ₂ C ₆ H ₃ CH=C(NO ₂)CH ₃ (50)	254
"	n-C ₄ H ₉ NO ₂	CH ₃ CO ₂ NH ₄	Boiling CH ₃ CO ₂ H	2,3-(CH ₃ O) ₂ C ₆ H ₃ CH=C(NO ₂)C ₂ H ₅ (60)	254
2,4-Dimethoxybenzaldehyde	CH ₃ NO ₂	CH ₃ CO ₂ NH ₄ /CH ₃ OH	Room	2,4-(CH ₃ O) ₂ C ₆ H ₃ CH=CHNO ₂ (80)	1009
"	"	CH ₃ CO ₂ NH ₄	Boiling CH ₃ CO ₂ H	2,4-(CH ₃ O) ₂ C ₆ H ₃ CH=CHNO ₂ (—)	1019
"	C ₂ H ₅ NO ₂	(C ₂ H ₅) ₂ NH	Room	2,4-(CH ₃ O) ₂ C ₆ H ₃ CH=C(NO ₂)CH ₃ (70)	769
"	"	n-C ₄ H ₉ NH ₂	Boiling C ₂ H ₅ OH	2,4-(CH ₃ O) ₂ C ₆ H ₃ CH=C(NO ₂)CH ₃ (79)	985
"	"	CH ₃ CO ₂ NH ₄	Boiling CH ₃ CO ₂ H	2,4-(CH ₃ O) ₂ C ₆ H ₃ CH=C(NO ₂)CH ₃ (85)	1019
"	C ₆ H ₅ CH ₂ NO ₂	CH ₃ NH ₂ Cl + Na ₂ CO ₃	Room	2,4-(CH ₃ O) ₂ C ₆ H ₃ CH=C(NO ₂)C ₆ H ₅ (—)	769
2,5-Dimethoxybenzaldehyde	CH ₃ NO ₂	"	"	2,5-(CH ₃ O) ₂ C ₆ H ₃ CH=CHNO ₂ (50)	1020
"	"	CH ₃ CO ₂ NH ₄	Boiling CH ₃ CO ₂ H	2,5-(CH ₃ O) ₂ C ₆ H ₃ CH=CHNO ₂ (—)	1019
"	C ₂ H ₅ NO ₂	"	"	2,5-(CH ₃ O) ₂ C ₆ H ₃ CH=C(NO ₂)CH ₃ (80)	1019
3,4-Dimethoxybenzaldehyde (veratraldehyde)	CH ₃ NO ₂	CH ₃ CO ₂ NH ₄ or CH ₃ NH ₂	Room	3,4-(CH ₃ O) ₂ C ₆ H ₃ CH=CHNO ₂ (80)	254, 1021
"	"	CH ₃ CO ₂ NH ₄	Boiling CH ₃ CO ₂ H	3,4-(CH ₃ O) ₂ C ₆ H ₃ CH=CHNO ₂ (70)	254, 1004, 1019

Note: References 285 to 1153 are on pp. 582-599.

§ The Schiff base from RCHO and n-butylamine was treated with acetic acid and nitro the compound.

TABLE XIII—Continued
CONDENSATIONS WITH ALIPHATIC NITRO COMPOUNDS



C. Aromatic Aldehydes—Continued					
Aldehyde	Nitro Compound	Catalyst	Temperature	Product(s) and Yield(s) (%)	Refs.
3,4-Dimethoxybenzaldehyde (veratraldehyde) (contd.)	CH ₃ NO ₂	C ₆ H ₅ CH ₂ NH ₂ -OCOCH ₃	50°	3,4-(CH ₃ O) ₂ C ₆ H ₃ CH=CHNO ₂ (82)	1022
"	C ₂ H ₅ NO ₂	(C ₂ H ₅) ₂ NH or n-C ₄ H ₉ NH ₂	Room	3,4-(CH ₃ O) ₂ C ₆ H ₃ CH=C(NO ₂)CH ₃ (75)	769, 1003, 1023
"	"	CH ₃ NH ₂ Cl + Na ₂ CO ₃	"	3,4-(CH ₃ O) ₂ C ₆ H ₃ CH=C(NO ₂)CH ₃ (54)	1002
"	"	CH ₃ CO ₂ NH ₄	Boiling CH ₃ CO ₂ H	3,4-(CH ₃ O) ₂ C ₆ H ₃ CH=C(NO ₂)CH ₃ (35)	254, 1019
"	n-C ₄ H ₉ NO ₂	"	"	3,4-(CH ₃ O) ₂ C ₆ H ₃ CH=C(NO ₂)C ₂ H ₅ (52)	254
"	C ₆ H ₅ CH ₂ NO ₂	CH ₃ NH ₂ Cl + Na ₂ CO ₃	Room	3,4-(CH ₃ O) ₂ C ₆ H ₃ CH=C(NO ₂)C ₆ H ₅ (Quant.)	769
"	"	§	—	3,4-(CH ₃ O) ₂ C ₆ H ₃ CH=C(NO ₂)C ₆ H ₅ (58)	28
3,5-Dimethoxybenzaldehyde	CH ₃ NO ₂	CH ₃ CO ₂ NH ₄	Boiling CH ₃ CO ₂ H	3,5-(CH ₃ O) ₂ C ₆ H ₃ CH=CHNO ₂ (—)	1019, 1024
"	C ₂ H ₅ NO ₂	"	"	3,5-(CH ₃ O) ₂ C ₆ H ₃ CH=C(NO ₂)CH ₃ (—)	1019
3,5-Dimethoxy-4-hydroxybenzaldehyde	CH ₃ NO ₂	CH ₃ NH ₂ /CH ₃ OH	Room	3,5-(CH ₃ O) ₂ -4-HOC ₆ H ₂ CH=CHNO ₂ (97)	1025
"	C ₂ H ₅ NO ₂	"	"	3,5-(CH ₃ O) ₂ -4-HOC ₆ H ₂ CH=C(NO ₂)CH ₃ (—)	1025
4-(CH ₃) ₂ NC ₆ H ₄ CHO	CH ₃ NO ₂	n-C ₄ H ₉ NH ₂ or H ₂ NCH ₂ CH ₂ NH ₂	"	4-(CH ₃) ₂ NC ₆ H ₄ CH=CHNO ₂ (83, 96)	283, 998
"	"	n-C ₄ H ₉ NH ₂	Steam bath	4-(CH ₃) ₂ NC ₆ H ₄ CH=CHNO ₂ (87)	1026
"	"	CH ₃ CO ₂ NH ₄	Boiling CH ₃ CO ₂ H	4-(CH ₃) ₂ NC ₆ H ₄ CH=CHNO ₂ (—)	1027
"	C ₂ H ₅ NO ₂	n-C ₄ H ₉ NH ₂ or H ₂ NCH ₂ CH ₂ NH ₂	Room or 50°	4-(CH ₃) ₂ NC ₆ H ₄ CH=C(NO ₂)CH ₃ (51)	283, 998
2-Nitro-5-methoxy-4-ethoxybenzaldehyde	n-C ₄ H ₉ NO ₂	n-C ₆ H ₁₁ NH ₂	Room	None	283
"	3-ClC ₆ H ₄ CH ₂ NO ₂	§	—	2-O ₂ N-5-CH ₃ O-4-C ₂ H ₅ OC ₆ H ₄ CH=C(NO ₂)C ₆ H ₄ Cl-3 (—)	987
4-i-C ₃ H ₇ C ₆ H ₄ CHO	CH ₃ NO ₂	CH ₃ NH ₂ Cl + Na ₂ CO ₃	Room	None	199
"	"	"	"	"	"
2,4,6-Trimethylbenzaldehyde	4-ClC ₆ H ₄ CH ₂ NO ₂	§	—	4-i-C ₃ H ₇ C ₆ H ₂ CH=C(NO ₂)C ₆ H ₄ Cl-4 (—)	987
"	C ₆ H ₅ CH ₂ NO ₂	§	—	2,4,6-(CH ₃) ₃ C ₆ H ₂ CH=C(NO ₂)C ₆ H ₅ (81)	28
2-Methoxy-3,5-dimethylbenzaldehyde	CH ₃ NO ₂	CH ₃ CO ₂ NH ₄	Boiling CH ₃ CO ₂ H	2-CH ₃ O-3,5-(CH ₃) ₂ C ₆ H ₂ CH=CHNO ₂ (—)	1027

2-Methoxy-4,5-dimethylbenzaldehyde	CH ₃ NO ₂	"	"	2-CH ₃ O-4,5-(CH ₃) ₂ C ₆ H ₃ CH=CHNO ₂ (—)	1027
2-Methoxy-4,6-dimethylbenzaldehyde	CH ₃ NO ₂	"	"	2-CH ₃ O-4,6-(CH ₃) ₂ C ₆ H ₃ CH=CHNO ₂ (—)	1017, 1028
4-Methoxy-2,6-dimethylbenzaldehyde	CH ₃ NO ₂	"	"	4-CH ₃ O-2,6-(CH ₃) ₂ C ₆ H ₃ CH=CHNO ₂ (—)	1017, 1028
2-Methoxy-5-ethylbenzaldehyde	CH ₃ NO ₂	"	"	2-CH ₃ O-5-C ₂ H ₅ C ₆ H ₃ CH=CHNO ₂ (—)	1024
4-Methoxy-5-ethylbenzaldehyde	CH ₃ NO ₂	"	"	4-CH ₃ O-5-C ₂ H ₅ C ₆ H ₃ CH=CHNO ₂ (—)	1024
4-Methoxy-2,3-dimethylbenzaldehyde	CH ₃ NO ₂	"	"	4-CH ₃ O-2,3-(CH ₃) ₂ C ₆ H ₃ CH=CHNO ₂ (—)	1024
4-Methoxy-3,5-dimethylbenzaldehyde	CH ₃ NO ₂	"	"	4-CH ₃ O-3,5-(CH ₃) ₂ C ₆ H ₃ CH=CHNO ₂ (—)	1024
4-Methoxy-3,6-dimethylbenzaldehyde	CH ₃ NO ₂	"	"	4-CH ₃ O-3,6-(CH ₃) ₂ C ₆ H ₃ CH=CHNO ₂ (—)	1024
2-Methoxy-3-ethoxybenzaldehyde	C ₂ H ₅ NO ₂	C ₂ H ₅ NH ₂ /C ₂ H ₅ OH	Room	2-CH ₃ O-3-C ₂ H ₅ OC ₆ H ₃ CH=C(NO ₂)CH ₃ (31)	1029
3-Methoxy-4-ethoxybenzaldehyde	CH ₃ NO ₂	n-C ₄ H ₉ NH ₂	"	3-CH ₃ O-4-C ₂ H ₅ OC ₆ H ₃ CH=CHNO ₂ (75)	1023
4-Methoxy-2-ethoxybenzaldehyde	CH ₃ NO ₂	CH ₃ CO ₂ NH ₄	Boiling CH ₃ CO ₂ H	3-CH ₃ O-4-C ₂ H ₅ OC ₆ H ₃ CH=CHNO ₂ (61)	1030
4-Methoxy-3-ethoxybenzaldehyde	CH ₃ NO ₂	CH ₃ CO ₂ NH ₄ /C ₂ H ₅ OH	Room	4-CH ₃ O-2-C ₂ H ₅ OC ₆ H ₃ CH=CHNO ₂ (80)	1009
4-Methoxy-2,3-dimethylbenzaldehyde	CH ₃ NO ₂	CH ₃ CO ₂ NH ₄	Boiling CH ₃ CO ₂ H	4-CH ₃ O-2-C ₂ H ₅ OC ₆ H ₃ CH=CHNO ₂ (—)	1017
2,4-Dimethoxy-3-methylbenzaldehyde	CH ₃ NO ₂	"	"	4-CH ₃ O-3-C ₂ H ₅ OC ₆ H ₃ CH=CHNO ₂ (—)	1027
2,4-Dimethoxy-6-methylbenzaldehyde	CH ₃ NO ₂	n-C ₄ H ₉ NH ₂	Room	4-CH ₃ O-3-C ₂ H ₅ OC ₆ H ₃ CH=C(NO ₂)CH ₃ (78)	1023
2,6-Dimethoxy-4-methylbenzaldehyde	CH ₃ NO ₂	CH ₃ CO ₂ NH ₄	Boiling CH ₃ CO ₂ H	2,4-(CH ₃ O) ₂ -3-CH ₃ C ₆ H ₃ CH=CHNO ₂ (—)	1027
3,4-Dimethoxy-6-methylbenzaldehyde	CH ₃ NO ₂	"	"	2,4-(CH ₃ O) ₂ -6-CH ₃ C ₆ H ₃ CH=CHNO ₂ (—)	1017, 1028
3-Methoxy-4-methoxy-methoxybenzaldehyde	CH ₃ NO ₂	CH ₃ NH ₂ Cl + Na ₂ CO ₃	Room	2,6-(CH ₃ O) ₂ -4-CH ₃ C ₆ H ₃ CH=CHNO ₂ (—)	1017
				3,4-(CH ₃ O) ₂ -6-CH ₃ C ₆ H ₃ CH=CHNO ₂ (—)	1027
				3-CH ₃ O-4-CH ₃ OCH ₂ OC ₆ H ₃ CH=CHNO ₂ (—)	910

Note: References 285 to 1153 are on pp. 582-599.

§ The Schiff base from RCHO and *n*-butylamine was treated with acetic acid and the nitro compound.

TABLE XIII—Continued
CONDENSATIONS WITH ALIPHATIC NITRO COMPOUNDS

C. Aromatic Aldehydes—Continued					
Aldehyde	Nitro Compound	Catalyst	Temperature	Product(s) and Yield(s) (%)	Refs.
2,3,5-Trimethoxybenzaldehyde	CH ₃ NO ₂	CH ₃ CO ₂ NH ₄	Boiling CH ₃ CO ₂ H	2,3,5-(CH ₃ O) ₃ C ₆ H ₂ CH=CHNO ₂ (—)	1017, 1028
2,3,6-Trimethoxybenzaldehyde	CH ₃ NO ₂	"	"	2,3,6-(CH ₃ O) ₃ C ₆ H ₂ CH=CHNO ₂ (—)	1017
2,4,6-Trimethoxybenzaldehyde	CH ₃ NO ₂	"	"	2,4,6-(CH ₃ O) ₃ C ₆ H ₂ CH=CHNO ₂ (85)	1028, 1032
3,4,5-Trimethoxybenzaldehyde	C ₆ H ₅ NO ₂	n-C ₄ H ₉ NH ₂ /C ₂ H ₅ OH	75°	2,4,6-(CH ₃ O) ₃ C ₆ H ₂ CH=C(NO ₂)CH ₃ (88)	1032
	CNCH ₃ NO ₂	CH ₃ NH ₂ Cl + Na ₂ CO ₃	Heat in C ₂ H ₅ OH	3,4,5-(CH ₃ O) ₃ C ₆ H ₂ CH=C(NO ₂)CN (95)	1033
	4-CH ₃ OC ₆ H ₄ -CH ₃ NO ₂	CH ₃ NH ₂ /alcohol	Room	3,4,5-(CH ₃ O) ₃ C ₆ H ₂ CH=C(NO ₂)C ₆ H ₄ OCH ₃ -4 (—)	212
				3,4,5-(CH ₃ O) ₃ C ₆ H ₂ CH[CH(NO ₂)C ₆ H ₄ OCH ₃ -4] ₂ (—)	
				3,4,5-(CH ₃ O) ₃ C ₆ H ₂  C ₆ H ₄ OCH ₃ -4 (—)	
				4-CH ₃ OC ₆ H ₄ 	
3,4,6-Trimethoxybenzaldehyde	CH ₃ NO ₂	CH ₃ CO ₂ NH ₄	Boiling CH ₃ CO ₂ H	3,4,6-(CH ₃ O) ₃ C ₆ H ₂ CH=CHNO ₂ (73)	1031
5-Bromo-8-nitro-1-naphthaldehyde	C ₆ H ₅ CH ₂ NO ₂	§	—	5-Br-8-O ₂ NC ₁₀ H ₆ [CH=C(NO ₂)C ₆ H ₅]-1 (—)	1034
5-Bromo-1-naphthaldehyde	C ₆ H ₅ CH ₂ NO ₂	§	—	5-BrC ₁₀ H ₆ [CH=C(NO ₂)C ₆ H ₅]-1 (—)	1034
4-Chloro-1-naphthaldehyde	4-O ₂ NC ₆ H ₄ CH ₂ NO ₂	§	—	4-ClC ₁₀ H ₆ [CH=C(NO ₂)C ₆ H ₄ NO ₂ -4']-1 (—)	1034
8-Nitro-1-naphthaldehyde	4-FC ₆ H ₄ CH ₂ NO ₂	§	—	8-O ₂ NC ₁₀ H ₆ [CH=C(NO ₂)C ₆ H ₄ F-2'] (—)	1034
1-Naphthaldehyde	C ₆ H ₅ CH ₂ NO ₂	§	—	1-C ₁₀ H ₇ CH=C(NO ₂)C ₆ H ₅ (68)	1034
2-Naphthaldehyde	C ₆ H ₅ CH ₂ NO ₂	§	—	2-C ₁₀ H ₇ CH=C(NO ₂)C ₆ H ₅ (—)	1034
3,4-Methylenedioxy-6-allylbenzaldehyde	CH ₃ NO ₂	CH ₃ NH ₂ Cl + Na ₂ CO ₃	—	3,4-CH ₂ O ₂ -6-C ₃ H ₅ C ₆ H ₂ CH=CHNO ₂ (69)	1035
4-Carbethoxymethoxybenzaldehyde	C ₆ H ₅ CH ₂ NO ₂	§	—	4-C ₂ H ₅ O ₂ CCH ₂ OC ₆ H ₄ CH=C(NO ₂)C ₆ H ₅ (52)	28

2-Ethoxy-4,6-dimethylbenzaldehyde	CH ₃ NO ₂	CH ₃ CO ₂ NH ₄	Boiling CH ₃ CO ₂ H	2-C ₂ H ₅ O-4,6-(CH ₃) ₂ C ₆ H ₂ CH=CHNO ₂ (—)	1017, 1028
4-Ethoxy-2,6-dimethylbenzaldehyde	CH ₃ NO ₂	"	"	4-C ₂ H ₅ O-2,6-(CH ₃) ₂ C ₆ H ₂ CH=CHNO ₂ (—)	1017, 1028
4-Ethoxy-2,3-dimethylbenzaldehyde	CH ₃ NO ₂	"	"	4-C ₂ H ₅ O-2,3-(CH ₃) ₂ C ₆ H ₂ CH=CHNO ₂ (—)	1024
4-Ethoxy-3,5-dimethylbenzaldehyde	CH ₃ NO ₂	"	"	4-C ₂ H ₅ O-3,5-(CH ₃) ₂ C ₆ H ₂ CH=CHNO ₂ (—)	1024
4-Ethoxy-3,6-dimethylbenzaldehyde	CH ₃ NO ₂	"	"	4-C ₂ H ₅ O-3,6-(CH ₃) ₂ C ₆ H ₂ CH=CHNO ₂ (—)	1024
3-Methoxy-2,4,6-trimethylbenzaldehyde	CH ₃ NO ₂	"	"	3-CH ₃ O-2,4,6-(CH ₃) ₃ C ₆ HCH=CHNO ₂ (—)	1024
4-Methoxy-2,3,6-trimethylbenzaldehyde	CH ₃ NO ₂	CH ₃ O ₂ CNH ₄	Boiling CH ₃ CO ₂ H	4-CH ₃ O-2,3,6-(CH ₃) ₃ C ₆ HCH=CHNO ₂ (—)	1024
3-Methoxy-2-propoxybenzaldehyde	CH ₃ NO ₂ C ₂ H ₅ NO ₂ n-C ₃ H ₇ NO ₂ i-C ₃ H ₇ CH ₂ NO ₂	CH ₃ NH ₂ /C ₂ H ₅ OH CH ₃ NH ₂ /CH ₃ OH CH ₃ NH ₂ CH ₃ NH ₂ /CH ₃ OH	Room " Boiling CH ₃ OH Room	3-CH ₃ O-2-n-C ₃ H ₇ OC ₆ H ₃ CH=CHNO ₂ (27) 3-CH ₃ O-2-n-C ₃ H ₇ OC ₆ H ₃ CH=C(NO ₂)CH ₃ (71) 3-CH ₃ O-2-n-C ₃ H ₇ OC ₆ H ₃ CH=C(NO ₂)C ₂ H ₅ (50) 3-CH ₃ O-2-n-C ₃ H ₇ OC ₆ H ₃ CH=C(NO ₂)C ₃ H ₇ -i (33)	1029 1029 1029 1029
3-Methoxy-2-isopropoxybenzaldehyde	CH ₃ NO ₂ C ₂ H ₅ NO ₂ n-C ₃ H ₇ NO ₂ CH ₃ NO ₂	CH ₃ NH ₂ /C ₂ H ₅ OH CH ₃ NH ₂ /CH ₃ OH CH ₃ NH ₂ CH ₃ NH ₂	" " Boiling CH ₃ OH 50°	3-CH ₃ O-2-i-C ₃ H ₇ OC ₆ H ₃ CH=CHNO ₂ (29) 3-CH ₃ O-2-i-C ₃ H ₇ OC ₆ H ₃ CH=C(NO ₂)CH ₃ (67) 3-CH ₃ O-2-i-C ₃ H ₇ OC ₆ H ₃ CH=C(NO ₂)C ₂ H ₅ (21) 2,3-(C ₂ H ₅ O) ₂ C ₆ H ₃ CH=CHNO ₂ (87)	1029 1029 1029 1022, 1036
2,3-Diethoxybenzaldehyde	CH ₃ NO ₂	C ₆ H ₅ CH ₂ NH ₂ + CH ₃ CO ₂ H/C ₂ H ₅ OH	Boiling CH ₃ CO ₂ H	2,4-(C ₂ H ₅ O) ₂ C ₆ H ₃ CH=CHNO ₂ (—)	1017
2,4-Diethoxybenzaldehyde	CH ₃ NO ₂	CH ₃ CO ₂ NH ₄	Boiling CH ₃ CO ₂ H	2,4-(C ₂ H ₅ O) ₂ C ₆ H ₃ CH=CHNO ₂ (—)	1017
3,4-Diethoxybenzaldehyde	CH ₃ NO ₂	CH ₃ NH ₂ Cl + Na ₂ CO ₃	Room	3,4-(C ₂ H ₅ O) ₂ C ₆ H ₃ CH=CHNO ₂ (94)	1037
2,4-Dimethoxy-3-ethylbenzaldehyde	C ₂ H ₅ NO ₂ CH ₃ NO ₂	n-C ₄ H ₉ NH ₂ CH ₃ CO ₂ NH ₄	" Boiling CH ₃ CO ₂ H	3,4-(C ₂ H ₅ O) ₂ C ₆ H ₃ CH=C(NO ₂)CH ₃ (44) 2,4-(CH ₃ O) ₂ -3-C ₂ H ₅ C ₆ H ₂ CH=CHNO ₂ (—)	1023 1027
2,4-Dimethoxy-5-ethylbenzaldehyde	CH ₃ NO ₂	"	"	2,4-(CH ₃ O) ₂ -5-C ₂ H ₅ C ₆ H ₂ CH=CHNO ₂ (—)	1024
3,4-Dimethoxy-6-ethylbenzaldehyde	CH ₃ NO ₂	"	"	3,4-(CH ₃ O) ₂ -6-C ₂ H ₅ C ₆ H ₂ CH=CHNO ₂ (—)	1027
4-Methoxy-2-ethoxy-6-methylbenzaldehyde	CH ₃ NO ₂	"	"	4-CH ₃ O-2-C ₂ H ₅ O-6-CH ₃ C ₆ H ₂ CH=CHNO ₂ (—)	1017, 1028

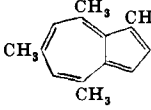
Note: References 285 to 1153 are on pp. 582-599.

§ The Schiff base from RCHO and *n*-butylamine was treated with acetic acid and the nitro compound.

TABLE XIII—Continued
CONDENSATIONS WITH ALIPHATIC NITRO COMPOUNDS

C. Aromatic Aldehydes—Continued

Aldehyde	Nitro Compound	Catalyst	Temperature	Product(s) and Yield(s) (%)	Refs.
3,5-Dimethoxy-4-ethoxybenzaldehyde	CH ₃ NO ₂	CH ₃ CO ₂ NH ₄	Boiling CH ₃ OH	3,5-(CH ₃ O) ₂ -4-C ₂ H ₅ OC ₆ H ₂ CH=CHNO ₂ (65)	1025
2,3,4,6-Tetramethoxybenzaldehyde	CH ₃ NO ₂	"	"	2,3,4,6-(CH ₃ O) ₄ C ₆ HCH=CHNO ₂ (93)	1038
4-Diethylamino-benzaldehyde	CH ₃ NO ₂ C ₂ H ₅ NO ₂	C ₆ H ₅ NH ₂ n-C ₄ H ₉ NH ₂	Water bath Heat, then room	4-(C ₂ H ₅) ₂ NC ₆ H ₄ CH=CHNO ₂ (70) 4-(C ₂ H ₅) ₂ NC ₆ H ₄ CH=C(NO ₂)CH ₃ (18)	985 985, 1026
5-Chloro-6-methoxy-2-naphthaldehyde	4-BrC ₆ H ₄ CH ₂ NO ₂	§	—	5-Cl-6-CH ₃ OC ₁₀ H ₆ [CH=C(NO ₂)C ₆ H ₄ Br-4']-2 (—)	1034
6-Nitro-2-methoxy-1-naphthaldehyde	3-BrC ₆ H ₄ CH ₂ NO ₂	§	—	6-O-N-2-CH ₃ OC ₁₀ H ₆ [CH=C(NO ₂)C ₆ H ₄ Br-3']-1 (—)	1034
4-Methyl-1-naphthaldehyde	3-O ₂ NC ₆ H ₄ CH ₂ NO ₂	§	—	4-CH ₃ C ₁₀ H ₆ [CH=C(NO ₂)C ₆ H ₄ NO ₂ -3']-1 (—)	1034
6-Methoxy-2-naphthaldehyde	4-ClC ₆ H ₄ CH ₂ NO ₂		—	6-CH ₃ OC ₁₀ H ₆ [CH=C(NO ₂)C ₆ H ₄ Cl-4']-2 (—)	1034
3-Methoxy-2- <i>n</i> -butoxybenzaldehyde	CH ₃ NO ₂ C ₂ H ₅ NO ₂ n-C ₃ H ₇ NO ₂	CH ₃ NH ₂ /C ₂ H ₅ OH CH ₃ NH ₂ /CH ₃ OH CH ₃ NH ₂	Room " Boiling CH ₃ OH	3-CH ₃ O-2-n-C ₄ H ₉ OC ₆ H ₃ CH=CHNO ₂ (20) 3-CH ₃ O-2-n-C ₄ H ₉ OC ₆ H ₃ CH=C(NO ₂)CH ₃ (53) 3-CH ₃ O-2-n-C ₄ H ₉ OC ₆ H ₃ CH=C(NO ₂)C ₂ H ₅ (36)	1029 1029 1029
3-Methoxy-2-isobutoxybenzaldehyde	C ₂ H ₅ NO ₂ n-C ₃ H ₇ NO ₂	CH ₃ NH ₂ /CH ₃ OH "	Room "	3-CH ₃ O-2-i-C ₄ H ₉ OC ₆ H ₃ CH=C(NO ₂)CH ₃ (34) 3-CH ₃ O-2-i-C ₄ H ₉ OC ₆ H ₃ CH=C(NO ₂)C ₂ H ₅ (57)	1029 1029
3-Ethoxy-2-propoxybenzaldehyde	C ₂ H ₅ NO ₂ i-C ₃ H ₇ CH ₂ NO ₂	" "	" "	3-C ₂ H ₅ O-2-n-C ₃ H ₇ OC ₆ H ₃ CH=CHNO ₂ (15) 3-C ₂ H ₅ O-2-i-C ₃ H ₇ OC ₆ H ₃ CH=CHNO ₂ (52)	1029 1029
3-Ethoxy-2-isopropoxybenzaldehyde	CH ₃ NO ₂ C ₂ H ₅ NO ₂ n-C ₃ H ₇ NO ₂	" " CH ₃ NH ₂	" " Boiling CH ₃ OH	3-C ₂ H ₅ O-2-i-C ₃ H ₇ OC ₆ H ₃ CH=C(NO ₂)CH ₃ (62) 3-C ₂ H ₅ O-2-i-C ₃ H ₇ OC ₆ H ₃ CH=C(NO ₂)C ₂ H ₅ (34)	1029 1029
2,4-Dimethoxy-5- <i>n</i> -propylbenzaldehyde	CH ₃ NO ₂	CH ₃ CO ₂ NH ₄	Boiling CH ₃ CO ₂ H	2,4-(CH ₃ O) ₂ -5-n-C ₃ H ₇ C ₆ H ₂ CH=CHNO ₂ (—)	1024
2,4-Diethoxy-3-methylbenzaldehyde	CH ₃ NO ₂	"	"	2,4-(C ₂ H ₅ O) ₂ -3-CH ₃ C ₆ H ₂ CH=CHNO ₂ (—)	1027
2,4-Diethoxy-6-methylbenzaldehyde	CH ₃ NO ₂	"	"	2,4-(C ₂ H ₅ O) ₂ -6-CH ₃ C ₆ H ₂ CH=CHNO ₂ (—)	1017
2,7-Dimethoxy-1-naphthaldehyde	2-ClC ₆ H ₄ CH ₂ NO ₂	§	—	2,7-(CH ₃ O) ₂ C ₁₀ H ₆ [CH=C(NO ₂)C ₆ H ₄ Cl-2']-1 (—)	1034

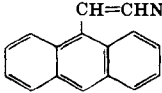
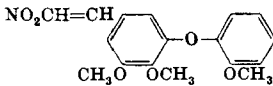
3-Methoxy-2- <i>n</i> -amyl- oxybenzaldehyde	CH ₃ NO ₂ C ₂ H ₅ NO ₂ <i>n</i> -C ₃ H ₇ NO ₂	CH ₃ NH ₂ /C ₂ H ₅ OH CH ₃ NH ₂ /CH ₃ OH CH ₃ NH ₂	Room " Boiling CH ₃ OH	3-CH ₃ O-2- <i>n</i> -C ₆ H ₁₁ OC ₆ H ₅ CH=CHNO ₂ (57) 1029 3-CH ₃ O-2- <i>n</i> -C ₆ H ₁₁ OC ₆ H ₅ CH=C(NO ₂)CH ₃ (48) 1029 3-CH ₃ O-2- <i>n</i> -C ₆ H ₁₁ OC ₆ H ₅ CH=C(NO ₂)C ₂ H ₅ (26) 1029
3-Methoxy-2-isoamyl- oxybenzaldehyde	CH ₃ NO ₂ C ₂ H ₅ NO ₂ <i>n</i> -C ₃ H ₇ NO ₂	CH ₃ NH ₂ /C ₂ H ₅ OH CH ₃ NH ₂ /CH ₃ OH CH ₃ NH ₂	Room " Boiling CH ₃ OH	3-CH ₃ O-2- <i>i</i> -C ₆ H ₁₁ OC ₆ H ₅ CH=CHNO ₂ (43) 1029 3-CH ₃ O-2- <i>i</i> -C ₆ H ₁₁ OC ₆ H ₅ CH=C(NO ₂)CH ₃ (48) 1029 3-CH ₃ O-2- <i>i</i> -C ₆ H ₁₁ OC ₆ H ₅ CH=C(NO ₂)C ₂ H ₅ (39) 1029
3-Ethoxy-2- <i>n</i> -butoxy- benzaldehyde	CH ₃ NO ₂ C ₂ H ₅ NO ₂	CH ₃ NH ₂ /C ₂ H ₅ OH CH ₃ NH ₂ /CH ₃ OH	Room "	3-C ₂ H ₅ O-2- <i>n</i> -C ₄ H ₉ OC ₆ H ₅ CH=CHNO ₂ (66) 1029 3-C ₂ H ₅ O-2- <i>n</i> -C ₄ H ₉ OC ₆ H ₅ CH=C(NO ₂)CH ₃ (60) 1029
3-Ethoxy-2-isobutoxy- benzaldehyde	C ₂ H ₅ NO ₂	"	"	3-C ₂ H ₅ O-2- <i>i</i> -C ₄ H ₉ OC ₆ H ₅ CH=CHNO ₂ (62) 1029
2,4-Diethoxy-5-ethyl- benzaldehyde	CH ₃ NO ₂	CH ₃ CO ₂ NH ₄	Boiling CH ₃ CO ₂ H	2,4-(C ₂ H ₅ O) ₂ -5-C ₂ H ₅ C ₆ H ₃ CH=CHNO ₂ (—) 1024
2,4,6-Triethoxybenzal- dehyde	CH ₃ NO ₂	"	"	2,4,6-(C ₂ H ₅ O) ₃ C ₆ H ₂ CH=CHNO ₂ (78) 1028, 1032
2-Nitro-5-benzyloxy- benzaldehyde	CH ₃ NO ₂	<i>n</i> -C ₆ H ₁₁ NH ₂	Room	2-O ₂ N-5-C ₆ H ₅ CH ₂ OC ₆ H ₅ CH=CHNO ₂ (—) 1039
4,6,8-Trimethylazulene- 1-carboxaldehyde	CH ₃ NO ₂	Piperidine/C ₂ H ₅ OH	"	 (41) 1040
3-Methoxy-2- <i>n</i> -hexyloxy- benzaldehyde	C ₂ H ₅ NO ₂	CH ₃ NH ₂ /CH ₃ OH	"	3-CH ₃ O-2- <i>n</i> -C ₆ H ₁₃ OC ₆ H ₅ CH=C(NO ₂)CH ₃ (64) 1029
3-Ethoxy-2- <i>n</i> -amyloxy- benzaldehyde	CH ₃ NO ₂ C ₂ H ₅ NO ₂	CH ₃ NH ₂ /C ₂ H ₅ OH "	" "	3-C ₂ H ₅ O-2- <i>n</i> -C ₅ H ₁₁ OC ₆ H ₅ CH=CHNO ₂ (47) 1029 3-C ₂ H ₅ O-2- <i>n</i> -C ₅ H ₁₁ OC ₆ H ₅ CH=C(NO ₂)CH ₃ (46) 1029
3-Ethoxy-2- isoamyloxy- benzaldehyde	C ₂ H ₅ NO ₂	"	"	3-C ₂ H ₅ O-2- <i>i</i> -C ₆ H ₁₁ OC ₆ H ₅ CH=C(NO ₂)CH ₃ (57) 1029
2,4-Diethoxy- 5- <i>n</i> -propyl- benzaldehyde	CH ₃ NO ₂	CH ₃ CO ₂ NH ₄	Boiling CH ₃ CO ₂ H	2,4-(C ₂ H ₅ O) ₂ -5- <i>n</i> -C ₃ H ₇ C ₆ H ₃ CH=CHNO ₂ (—) 1024

Note: References 285 to 1153 are on pp. 582-599.

§ The Schiff base from RCHO and *n*-butylamine was treated with acetic acid and the nitro compound.


|| The Schiff base from RCHO and *n*-propylamine was treated with acetic acid and the nitro compound.

TABLE XIII—Continued
CONDENSATIONS WITH ALIPHATIC NITRO COMPOUNDS

C. Aromatic Aldehydes—Continued					
Aldehyde	Nitro Compound	Catalyst	Temperature	Product(s) and Yield(s) (%)	Refs.
Anthracene-9- carboxaldehyde	CH ₃ NO ₂	<i>n</i> -C ₆ H ₁₁ NH ₂ /C ₂ H ₅ OH	2°	 (72) 986	
3-Methoxy-2-benzyl- oxybenzaldehyde	CH ₃ NO ₂	<i>n</i> -C ₆ H ₁₁ NH ₂ /C ₂ H ₅ OH	Room	3-CH ₃ O-2-C ₆ H ₅ CH ₂ OC ₆ H ₅ CH=CHNO ₂ (59) 1041	
3-Methoxy-4-benzyl- oxybenzaldehyde	CH ₃ NO ₂	CH ₃ CO ₂ NH ₄ CH ₃ NH ₂ , or CH ₃ NH ₂ Cl + Na ₂ CO ₃	Boiling CH ₃ CO ₂ H Room	3-CH ₃ O-2-C ₆ H ₅ CH ₂ OC ₆ H ₅ CH=CHNO ₂ (—) 1028 3-CH ₃ O-4-C ₆ H ₅ CH ₂ OC ₆ H ₅ CH=CHNO ₂ (96) 910, 1002, 1015	
4-Methoxy-2-benzyl- oxybenzaldehyde	CH ₃ NO ₂	CH ₃ CO ₂ NH ₄	Boiling CH ₃ CO ₂ H	4-CH ₃ O-2-C ₆ H ₅ CH ₂ OC ₆ H ₅ CH=CHNO ₂ (—) 1017	
3,4-Dimethoxy-5-phen- oxybenzaldehyde	CH ₃ NO ₂	CH ₃ CO ₂ NH ₄ + CH ₃ CO ₂ H	Boiling CH ₃ NO ₂	3,4-(CH ₃ O) ₂ -5-C ₆ H ₅ OC ₆ H ₂ CH=CHNO ₂ (72) 1042	
3-Ethoxy-2- <i>n</i> -hexyloxy- benzaldehyde	<i>n</i> -C ₃ H ₇ NO ₂	CH ₃ NH ₂	Boiling CH ₃ OH	3-C ₂ H ₅ O-2- <i>n</i> -C ₆ H ₁₃ OC ₆ H ₅ CH=C(NO ₂)C ₂ H ₅ (37) 1029	
2,4-Dimethoxy-5- <i>n</i> - hexylbenzaldehyde	CH ₃ NO ₂	CH ₃ CO ₂ NH ₄	Boiling CH ₃ CO ₂ H	2,4-(CH ₃ O) ₂ -5- <i>n</i> -C ₆ H ₁₃ C ₆ H ₂ CH=CHNO ₂ (—) 1024	
2,4-Dimethoxy-3- benzylbenzaldehyde	CH ₃ NO ₂	"	"	2,4-(CH ₃ O) ₂ -3-C ₆ H ₅ CH ₂ C ₆ H ₄ CH=CHNO ₂ (—) 1027	
3,5-Dimethoxy-4- benzyloxy- benzaldehyde	CH ₃ NO ₂	CH ₃ NH ₂ Cl + Na ₂ CO ₃	40°	3,5-(CH ₃ O) ₂ -4-C ₆ H ₅ CH ₂ OC ₆ H ₂ CH=CHNO ₂ (65) 1043	
3-Methoxy-2- <i>n</i> -octyloxy- benzaldehyde	C ₂ H ₅ NO ₂	CH ₃ NH ₂	Boiling CH ₃ OH	3-CH ₃ O-2- <i>n</i> -C ₈ H ₁₇ OC ₆ H ₅ CH=C(NO ₂)CH ₃ (63) 1029	
3,4-Dimethoxy-5-(2'- methoxy-4'-formyl- phenoxy)- benzaldehyde	CH ₃ NO ₂	CH ₃ CO ₂ NH ₄	Boiling CH ₃ CO ₂ H	 (57) 1016	

3-Methoxy-2- <i>n</i> -nonyl- oxybenzaldehyde	$n\text{-C}_9\text{H}_{19}\text{NO}_2$	CH_3NH_2	Boiling CH_3OH	$3\text{-CH}_3\text{O-2-}n\text{-C}_9\text{H}_{19}\text{OC}_6\text{H}_5\text{CH}=\text{C}(\text{NO}_2)\text{C}_2\text{H}_5$ (36)	1029
3-Ethoxy-2- <i>n</i> -octyloxy- benzaldehyde	$\text{C}_2\text{H}_5\text{NO}_2$	"	"	$3\text{-C}_2\text{H}_5\text{O-2-}n\text{-C}_8\text{H}_{17}\text{OC}_6\text{H}_5\text{CH}=\text{C}(\text{NO}_2)\text{CH}_3$ (69)	1029
2,4-Diethoxy-5- <i>n</i> - hexylbenzaldehyde	CH_3NO_2	$\text{CH}_3\text{CO}_2\text{NH}_4$	Boiling $\text{CH}_3\text{CO}_2\text{H}$	$2,4\text{-(C}_2\text{H}_5\text{O)}_2\text{-5-}n\text{-C}_6\text{H}_{13}\text{C}_6\text{H}_2\text{CH}=\text{CHNO}_2$ (—)	1024
2,4-Dimethoxy-6- benzyloxy-5- acetylbenzaldehyde	CH_3NO_2	Piperidine + pyridine	100°	$2,4\text{-(CH}_3\text{O)}_2\text{-6-C}_6\text{H}_5\text{CH}_2\text{O-5-CH}_3\text{COC}_6\text{H}_4\text{CH}=\text{CHNO}_2$ (45)	574
	"	Piperidine/ CH_3OH	Room	$2,4\text{-(CH}_3\text{O)}_2\text{-6-C}_6\text{H}_5\text{CH}_2\text{O-5-CH}_3\text{COC}_6\text{H}_4\text{CH}(\text{CH}_2\text{NO}_2)_2$ (8)	574
2,4-Diethoxy-3- benzylbenzaldehyde	CH_3NO_2	$\text{CH}_3\text{CO}_2\text{NH}_4$	Boiling $\text{CH}_3\text{CO}_2\text{H}$	$2,4\text{-(C}_2\text{H}_5\text{O)}_2\text{-3-C}_6\text{H}_5\text{CH}_2\text{C}_6\text{H}_2\text{CH}=\text{CHNO}_2$ (—)	1027
3-Ethoxy-2- <i>n</i> -nonyl- oxybenzaldehyde	$n\text{-C}_9\text{H}_{19}\text{NO}_2$	CH_3NH_2	Boiling CH_3OH	$3\text{-C}_2\text{H}_5\text{O-2-}n\text{-C}_9\text{H}_{19}\text{OC}_6\text{H}_5\text{CH}=\text{C}(\text{NO}_2)\text{C}_2\text{H}_5$ (31)	1029
2-Nitro-4,5-dibenzyl- oxybenzaldehyde	CH_3NO_2	$n\text{-C}_6\text{H}_{11}\text{NH}_2$	Room	$2\text{-O}_2\text{N-4,5-(C}_6\text{H}_5\text{CH}_2\text{O)}_2\text{C}_6\text{H}_2\text{CH}=\text{CHNO}_2$ (—)	1039
3,4-Dibenzoyloxy- benzaldehyde	CH_3NO_2	"	"	$3,4\text{-(C}_6\text{H}_5\text{CH}_2\text{O)}_2\text{C}_6\text{H}_2\text{CH}=\text{CHNO}_2$ (50)	1039
	"	$\text{CH}_3\text{CO}_2\text{NH}_4$	Boiling $\text{CH}_3\text{CO}_2\text{H}$	$3,4\text{-(C}_6\text{H}_5\text{CH}_2\text{O)}_2\text{C}_6\text{H}_2\text{CH}=\text{CHNO}_2$ (—)	1027
	"	"	"	$3,4\text{-(C}_6\text{H}_5\text{CH}_2\text{O)}_2\text{C}_6\text{H}_2\text{CH}=\text{CHNO}_2$ (80)	1044
	$\text{C}_2\text{H}_5\text{NO}_2$	$n\text{-C}_6\text{H}_{11}\text{NH}_2$	Room	$3,4\text{-(C}_6\text{H}_5\text{CH}_2\text{O)}_2\text{C}_6\text{H}_2\text{CH}=\text{C}(\text{NO}_2)\text{CH}_3$ (—)	1039
	$n\text{-C}_9\text{H}_{19}\text{NO}_2$	"	"	$3,4\text{-(C}_6\text{H}_5\text{CH}_2\text{O)}_2\text{C}_6\text{H}_2\text{CH}=\text{C}(\text{NO}_2)\text{C}_2\text{H}_5$ (—)	1039
3-Ethoxy-2-dodecyl- oxybenzaldehyde	$\text{C}_2\text{H}_5\text{NO}_2$	CH_3NH_2	Boiling CH_3OH	$3\text{-C}_2\text{H}_5\text{O-2-}n\text{-C}_{12}\text{H}_{25}\text{OC}_6\text{H}_5\text{CH}=\text{C}(\text{NO}_2)\text{CH}_3$ (77)	1029




D. Heterocyclic Aldehydes or Ketones

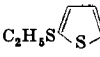
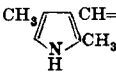
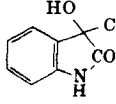
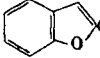
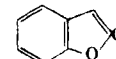
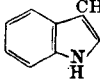
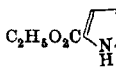
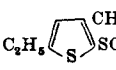
Aldehyde or Ketone					
Thiazole-4- carboxaldehyde	CH_3NO_2	$n\text{-C}_4\text{H}_9\text{NH}_2$ / $\text{C}_2\text{H}_5\text{OH}$	Room	 (—)	1045
Thiophene-2- carboxaldehyde	$\text{C}_2\text{H}_5\text{NO}_2$	$n\text{-C}_5\text{H}_{11}\text{NH}_2$	25°	$2\text{-C}_4\text{H}_9\text{SCH}=\text{C}(\text{NO}_2)\text{CH}_3$ (73)	1046
	$n\text{-C}_3\text{H}_7\text{NO}_2$	"	25°	$2\text{-C}_4\text{H}_9\text{SCH}=\text{C}(\text{NO}_2)\text{C}_2\text{H}_5$ (52)	1046
	$\text{C}_6\text{H}_5\text{CH}_2\text{NO}_2$	CH_3NH_2 / CH_3OH	Room	$2\text{-C}_4\text{H}_9\text{SCH}=\text{C}(\text{NO}_2)\text{C}_6\text{H}_5$ (30)	1047
	"	§	—	$2\text{-C}_4\text{H}_9\text{SCH}=\text{C}(\text{NO}_2)\text{C}_6\text{H}_5$ (81)	28

Note: References 285 to 1153 are on pp. 582-599.

§ The Schiff base from RCHO and *n*-butylamine was treated with acetic acid and the nitro compound.

TABLE XIII—Continued
CONDENSATIONS WITH ALIPHATIC NITRO COMPOUNDS

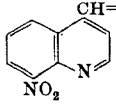
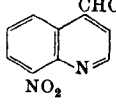
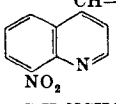
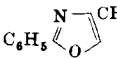
D. Heterocyclic Aldehydes or Ketones—Continued					
Aldehyde or Ketone	Nitro Compound	Catalyst	Temperature	Product(s) and Yield(s) (%)	Refs.
Furfural	$\text{C}_2\text{H}_5\text{NO}_2$	$n\text{-C}_4\text{H}_9\text{NH}_2$	Boiling $\text{C}_2\text{H}_5\text{OH}$	$2\text{-C}_4\text{H}_9\text{OCH}=\text{C}(\text{NO}_2)\text{CH}_3$ (85-90)	996
	$n\text{-C}_3\text{H}_7\text{NO}_2$	"	"	$2\text{-C}_4\text{H}_9\text{OCH}=\text{C}(\text{NO}_2)\text{C}_2\text{H}_5$ (90)	996
	$n\text{-C}_4\text{H}_9\text{NO}_2$	"	"	$2\text{-C}_4\text{H}_9\text{OCH}=\text{C}(\text{NO}_2)\text{C}_2\text{H}_5$ (90)	996
	$\text{C}_2\text{H}_5\text{O}_2\text{CCH}_2\text{NO}_2$	$(\text{C}_2\text{H}_5)_2\text{NH}$	20°	$2\text{-C}_4\text{H}_9\text{OCH}[\text{CH}(\text{NO}_2)\text{CO}_2\text{C}_2\text{H}_5]_2$ (82)	990
	$2\text{-ClC}_6\text{H}_4\text{CH}_2\text{NO}_2$	CH_3NH_2 / CH_3OH	Room	$2\text{-C}_4\text{H}_9\text{OCH}=\text{C}(\text{NO}_2)\text{C}_6\text{H}_4\text{Cl-2}$ (25)	1047
	"	§	—	$2\text{-C}_4\text{H}_9\text{OCH}=\text{C}(\text{NO}_2)\text{C}_6\text{H}_4\text{Cl-2}$ (82)	28
	$\text{C}_6\text{H}_5\text{CH}_2\text{NO}_2$	§	—	$2\text{-C}_4\text{H}_9\text{OCH}=\text{C}(\text{NO}_2)\text{C}_6\text{H}_5$ (81)	28
4-Methylthiazole-5- carboxaldehyde	CH_3NO_2	$n\text{-C}_4\text{H}_9\text{NH}_2$ / CH_3OH	Room	 (—)	1048
	$\text{C}_2\text{H}_5\text{NO}_2$	"	"	 (—)	1048
Pyridine-2-carbox- aldehyde	$\text{C}_2\text{H}_5\text{O}_2\text{CCH}_2\text{NO}_2$	$(\text{C}_2\text{H}_5)_2\text{NH}$	20°	$2\text{-C}_5\text{H}_4\text{NCH}[\text{CH}(\text{NO}_2)\text{CO}_2\text{C}_2\text{H}_5]_2$ (81)	990
	$\text{C}_6\text{H}_5\text{CH}_2\text{NO}_2$	$(\text{C}_2\text{H}_5)_2\text{NH}$ or $(\text{C}_2\text{H}_5)_3\text{N}/\text{C}_2\text{H}_5\text{OH}$	Room	$2\text{-C}_5\text{H}_4\text{NCHOHCH}(\text{NO}_2)\text{C}_6\text{H}_5$ (87)	1049
Pyridine-3-carboxalde- hyde	CH_3NO_2	$\text{CH}_3\text{NH}_2\text{Cl} + \text{Na}_2\text{CO}_3$	"	$3\text{-C}_5\text{H}_4\text{NCH}=\text{CHNO}_2$ (—)	168, 1050
	$\text{C}_6\text{H}_5\text{CH}_2\text{NO}_2$	"	"	$3\text{-C}_5\text{H}_4\text{NCH}[\text{CH}(\text{NO}_2)\text{C}_6\text{H}_5]_2$ (25)	168
	"	$(\text{C}_2\text{H}_5)_2\text{NH}$ or $(\text{C}_2\text{H}_5)_3\text{N}/\text{C}_2\text{H}_5\text{OH}$	Room	$3\text{-C}_5\text{H}_4\text{NCHOHCH}(\text{NO}_2)\text{C}_6\text{H}_5$ (87)	1049
Pyridine-4-carboxal- dehyde	$\text{C}_6\text{H}_5\text{CH}_2\text{NO}_2$	"	"	$4\text{-C}_5\text{H}_4\text{NCHOHCH}(\text{NO}_2)\text{C}_6\text{H}_5$ (88)	1049
Pyridine-2,6-dicarbox- aldehyde	$\text{C}_6\text{H}_5\text{CH}_2\text{NO}_2$	"	"	$\text{C}_5\text{H}_3\text{N}[\text{CHOHCH}(\text{NO}_2)\text{C}_6\text{H}_5]_2\text{-2,6}$ (80)	1049
6-Methylpyridine-2- carboxaldehyde	$\text{C}_6\text{H}_5\text{CH}_2\text{NO}_2$	"	"	$6\text{-CH}_3\text{C}_5\text{H}_3\text{NCHOHCH}(\text{NO}_2)\text{C}_6\text{H}_5\text{-2}$ (90)	1049
3-Ethylthiophene-2- carboxaldehyde	CH_3NO_2	$\text{CH}_3\text{NH}_2\text{Cl}$ + Na_2CO_3	"	 (52)	1051

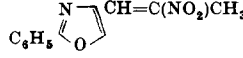
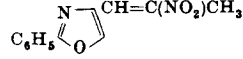
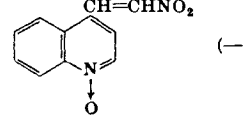
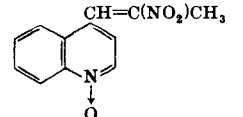
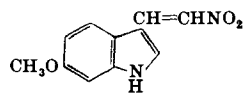
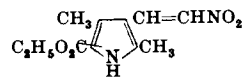
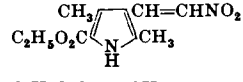
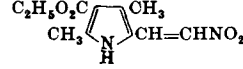
5-Ethylthiophene-2-carboxaldehyde	CH ₃ NO ₂	"	"		1051
2,4-Dimethylpyrrole-3-carboxaldehyde	CH ₃ NO ₂	"	"		779
Isatin	CH ₃ NO ₂ C ₆ H ₅ NO ₂ n-C ₃ H ₇ NO ₂	(C ₂ H ₅) ₂ NH " "	Cool " "	 (R = H, 71) (R = CH ₃ , 80) (R = C ₂ H ₅ , 74)	1052 1052 1052
4,6-Dimethylpyridine-2-carboxaldehyde	C ₄ H ₅ CH ₂ NO ₂	(C ₂ H ₅) ₂ NH or (C ₂ H ₅) ₃ N/C ₂ H ₅ OH	Room	4,6-(CH ₃) ₂ C ₅ H ₂ NCHOHCH(NO ₂)C ₆ H ₅ ·2 (95)	1049
Benzofuran-2-carboxaldehyde	CH ₃ NO ₂	(CH ₃) ₃ NHCl + Na ₂ CO ₃	—		1053
	C ₄ H ₅ NO ₂	"	—		1053
Indole-3-carboxaldehyde	C ₂ H ₅ NO ₂	C ₆ H ₅ CH ₂ NH ₂	Boiling C ₂ H ₅ NO ₂		213
Ethyl 2-methyl-3-formylpyrrole-5-carboxylate	CH ₃ NO ₂	CH ₃ NH ₂	Boiling C ₂ H ₅ OH		654
2-Ethylthio-5-ethylthiophene-3-carboxaldehyde	CH ₃ NO ₂	CH ₃ NH ₂ Cl + Na ₂ CO ₃	Room		1051

Note: References 285 to 1153 are on pp. 582-599.

§ The Schiff base from RCHO and n-butylamine was treated with acetic acid and the nitro compound.

TABLE XIII—Continued
CONDENSATIONS WITH ALIPHATIC NITRO COMPOUNDS

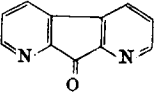
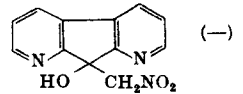
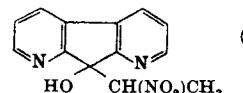
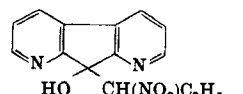
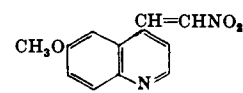
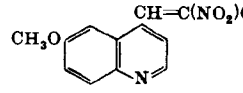
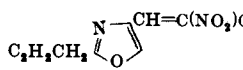
D. Heterocyclic Aldehydes or Ketones—Continued					
Aldehyde or Ketone	Nitro Compound	Catalyst	Temperature	Product(s) and Yield(s) (%)	Refs.
8-Nitroquinoline-4-carboxaldehyde	CH ₃ NO ₂	§	—		1054
	C ₂ H ₅ NO ₂	(C ₂ H ₅) ₂ NH/C ₂ H ₅ OH	Room		1055
	"	§	—		1054
Quinoline-4-carboxaldehyde hydrate	CH ₃ NO ₂	(C ₂ H ₅) ₂ NH/ aq. ethanol	Room	4-C ₉ H ₆ NCHOHCH ₂ NO ₂ (93)	42
	"	n-C ₄ H ₉ NH ₂ /CH ₃ OH	Refrigerator	4-C ₉ H ₆ NCH=CHNO ₂ (—)	1056
	"	§	—	4-C ₉ H ₆ NCH=CHNO ₂ (—)	1054
	C ₂ H ₅ NO ₂	(C ₂ H ₅) ₂ NH/ aq. ethanol	Room	4-C ₉ H ₆ NCHOHCH(NO ₂)CH ₃ (95)	42
	n-C ₃ H ₇ NO ₂	"	"	4-C ₉ H ₆ NCHOHCH(NO ₂)C ₂ H ₅ (Quant.)	42
	n-C ₄ H ₉ NO ₂	"	"	4-C ₉ H ₆ NCHOHCH(NO ₂)C ₃ H ₇ -n (95)	42
Quinoline-8-carboxaldehyde	CH ₃ NO ₂	n-C ₆ H ₁₁ NH ₂	Refrigerator	8-C ₉ H ₆ NCH=CHNO ₂ (—)	1056
Isoquinoline-7-carboxaldehyde	CH ₃ NO ₂	§	—	8-C ₉ H ₆ NCH=CHNO ₂ (—)	1054
	"	C ₆ H ₅ N(CH ₃) ₂	Room	7-C ₉ H ₆ NCHOHCH ₂ NO ₂ (55)	203
2-Phenylloxazole-4-carboxaldehyde	CH ₃ NO ₂	CH ₃ CO ₂ NH ₄	Boiling CH ₃ NO ₂		633

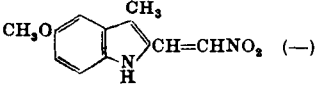
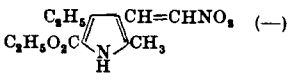
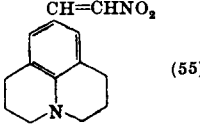
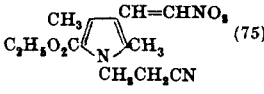
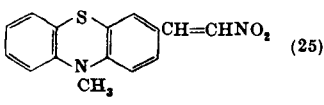
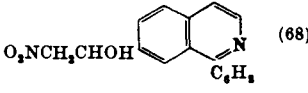
	$C_2H_5NO_2$	„	Boiling $C_2H_5NO_2$	 (80)	633
	„	$n-C_4H_9NH_2$	Room	 (47)	633
Quinoline-N-oxide-4-carboxaldehyde	CH_3NO_2	§	—	 (—)	1054
	$C_2H_5NO_2$	§	—	 (—)	1054
6-Methoxyindole-3-carboxaldehyde	CH_3NO_2	Piperidine	Boiling C_6H_6	 (42)	1057
Ethyl 2,4-dimethyl-3-formylpyrrole-5-carboxaldehyde	CH_3NO_2	$CH_3NH_2Cl + Na_2CO_3$	Room	 (—)	913
	$HO_2CCH_2NO_2$	„	„	 (—)	913
Ethyl 2,4-dimethyl-5-formylpyrrole-3-carboxylate	CH_3NO_2	„	„	 (—)	913

Note: References 285 to 1153 are on pp. 582-599.

§ The Schiff base from RCHO and *n*-butylamine was treated with acetic acid and the nitro compound.

TABLE XIII—Continued
CONDENSATIONS WITH ALIPHATIC NITRO COMPOUNDS

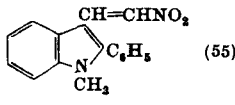
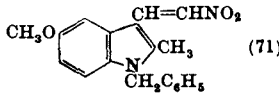
D. Heterocyclic Aldehydes or Ketones—Continued					
Aldehyde or Ketone	Nitro Compound	Catalyst	Temperature	Product(s) and Yield(s) (%)	Refs.
	CH_3NO_2	Piperidine	50°	 (—)	1058
	$C_2H_5NO_2$	„	50°	 (—)	1058
	$n-C_3H_7NO_2$	„	50°	 (—)	1058
6-Methoxyquinoline-4-carboxaldehyde	CH_3NO_2	§	—	 (—)	1054
	$C_2H_5NO_2$	§	—	 (—)	1054
2-Benzylloxazole-4-carboxaldehyde	$C_2H_5NO_2$	$n-C_4H_9NH_2$	Room	 (23)	1059

5-Methoxy-3-methylindole-2-carboxaldehyde	CH_3NO_2	$n\text{-C}_4\text{H}_9\text{NH}_2 / \text{CH}_3\text{OH}$	"		1060
Ethyl 2-methyl-4-ethyl-3-formylpyrrole-5-carboxylate	CH_3NO_2	$\text{CH}_3\text{NH}_2\text{Cl} + \text{Na}_2\text{CO}_3$	"		644
Julolidine-9-carboxaldehyde	CH_3NO_2	$n\text{-C}_6\text{H}_{11}\text{NH}_2$	Steam bath, then room		1026
Ethyl 1-(2'-cyanoethyl)-2,4-dimethyl-3-formylpyrrole-5-carboxylate	CH_3NO_2	CH_3NH_2	Boiling $\text{C}_2\text{H}_5\text{OH}$		654
10-Methylpheno-thiazine-3-carboxaldehyde	CH_3NO_2	$\text{CH}_3\text{CO}_2\text{NH}_4$	Boiling $\text{CH}_3\text{CO}_2\text{H}$		658
1-Phenyl-isoquinoline-7-carboxaldehyde	CH_3NO_2	$\text{C}_4\text{H}_9\text{N}(\text{CH}_3)_2$	Room		203

Note: References 285 to 1153 are on pp. 582-599.

§ The Schiff base from RCHO and *n*-butylamine was treated with acetic acid and the nitro compound.

TABLE XIII—Continued
CONDENSATIONS WITH ALIPHATIC NITRO COMPOUNDS

D. Heterocyclic Aldehydes or Ketones—Continued					
Aldehyde or Ketone	Nitro Compound	Catalyst	Temperature	Product(s) and Yield(s) (%)	Refs.
5-Benzylxyindole-3-carboxaldehyde	CH_3NO_2	$\text{C}_4\text{H}_9\text{CH}_2\text{NH}_2$	Boiling CH_3NO_2	$5\text{-C}_6\text{H}_5\text{CH}_2\text{OC}_6\text{H}_4\text{N-3-CH=CHNO}_2$ (80)	213
	$\text{C}_2\text{H}_5\text{NO}_2$	"	"	$5\text{-C}_6\text{H}_5\text{CH}_2\text{OC}_6\text{H}_4\text{N-3-CH=C(NO}_2\text{)CH}_3$ (81)	213
	$n\text{-C}_3\text{H}_7\text{NO}_2$	"	Boiling $n\text{-C}_3\text{H}_7\text{NO}_2$	$5\text{-C}_6\text{H}_5\text{CH}_2\text{OC}_6\text{H}_4\text{N-3-CH=C(NO}_2\text{)C}_2\text{H}_5$ (57)	213
1-Methyl-2-phenylindole-3-carboxaldehyde	CH_3NO_2	$n\text{-C}_4\text{H}_9\text{NH}_2$	Steam bath		924
1-Benzyl-2-methyl-5-methoxyindole-3-carboxaldehyde	CH_3NO_2	$\text{CH}_3\text{CO}_2\text{NH}_4$	Boiling CH_3NO_2		1061

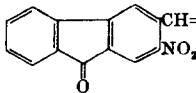
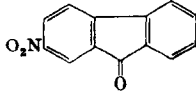
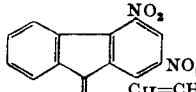
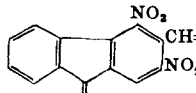
Note: References 285 to 1153 are on pp. 582-599.

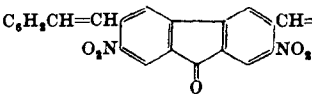
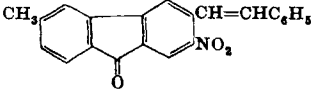
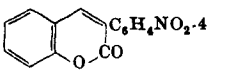
TABLE XIV
CONDENSATIONS WITH AROMATIC NITRO COMPOUNDS

A. <i>Alkyl Ketone</i>					
Aldehyde or Ketone	Nitro compound	Catalyst	Temperature	Product(s) and Yield(s) (%)	Refs.
1,3-Diphenylpropanetrione	4-O ₂ NC ₆ H ₄ CH ₂ CN	Piperidine + pyridine	Room	(C ₆ H ₅ CO) ₂ C(OH)CH(CN)C ₆ H ₄ NO ₂ -4 (43)	352
B. <i>Aromatic Aldehydes</i>					
4-Chlorobenzaldehyde	2,4,6-(O ₂ N) ₃ C ₆ H ₂ CH ₃	Piperidine	120°	4-ClC ₆ H ₄ CH=CHC ₆ H ₂ (NO ₂) ₃ -2,4,6 (32)	1062
2-Nitrobenzaldehyde	2,4-(O ₂ N) ₂ C ₆ H ₃ CH ₃	"	160°, then 130-140°	2-O ₂ NC ₆ H ₄ CH=CHC ₆ H ₃ (NO ₂) ₂ -2,4 (40)	1063
3-Nitrobenzaldehyde	2,4,6-(O ₂ N) ₃ C ₆ H ₂ CH ₃	"	Boiling C ₆ H ₆	2-O ₂ NC ₆ H ₄ CH=CHC ₆ H ₂ (NO ₂) ₃ -2,4,6 (—)	1064
	2,4-(O ₂ N) ₂ C ₆ H ₃ CH ₃	"	160°, then 130-140°	3-O ₂ NC ₆ H ₄ CH=CHC ₆ H ₃ (NO ₂) ₂ -2,4 (90)	1063, 1065
4-Nitrobenzaldehyde	2,4,6-(O ₂ N) ₃ C ₆ H ₂ CH ₃	"	Boiling C ₆ H ₆	3-O ₂ NC ₆ H ₄ CH=CHC ₆ H ₂ (NO ₂) ₃ -2,4,6 (—)	1064
	2,4-(O ₂ N) ₂ C ₆ H ₃ CH ₃	CH ₃ CO ₂ NH ₄	Boiling C ₂ H ₅ OH	3-O ₂ NC ₆ H ₄ CH=C(CO ₂ C ₂ H ₅)-C ₆ H ₃ (NO ₂) ₂ -2,4 (50)	217
4-Nitrobenzaldehyde	2,4-(O ₂ N) ₂ C ₆ H ₃ CH ₃	Piperidine	160°, then 130-140°	4-O ₂ NC ₆ H ₄ CH=CHC ₆ H ₃ (NO ₂) ₂ -2,4 (80)	1063
Benzaldehyde	2,4,6-(O ₂ N) ₃ C ₆ H ₂ CH ₃	Piperidine/alcohol	40°	4-O ₂ NC ₆ H ₄ CH=CHC ₆ H ₂ (NO ₂) ₃ -2,4,6 (70)	218
	4-O ₂ NC ₆ H ₄ CH ₂ CO ₂ H	CH ₃ CO ₂ NH ₄	Boiling CH ₃ CO ₂ H	C ₆ H ₅ CH=C(CO ₂ H)C ₆ H ₄ NO ₂ -4 (Small)	217
	2,4-(O ₂ N) ₂ C ₆ H ₃ CH ₃	Piperidine	160°; boiling CH ₃ OH	C ₆ H ₅ CH=CHC ₆ H ₃ (NO ₂) ₂ -2,4 (65; 90)	225, 1063
	2,6-(O ₂ N) ₂ C ₆ H ₃ CH ₃	"	130° or 170°	C ₆ H ₅ CH=CHC ₆ H ₃ (NO ₂) ₂ -2,6 (30)	1065, 1066
	"	"	B.p.	C ₆ H ₅ CH=CHC ₆ H ₃ (NO ₂) ₂ -2,6 (75)	1067
	2-O ₂ N-4-NCC ₆ H ₃ CH ₃	"	140-160°	C ₆ H ₅ CH=CHC ₆ H ₃ CN-4-NO ₂ -2 (75)	218
	4-O ₂ N-2-NCC ₆ H ₃ CH ₃	"	120-140°	C ₆ H ₅ CH=CHC ₆ H ₃ CN-2-NO ₂ -4 (75)	218
	2-O ₂ N-4-H ₂ NO ₂ SC ₆ H ₃ CH ₃	"	150-160°	C ₆ H ₅ CH=CHC ₆ H ₃ NO ₂ -2-SO ₂ NH ₂ -4 (40)	218

Note: References 285 to 1153 are on pp. 582-599.

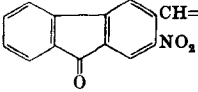
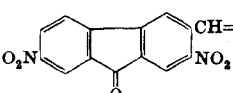
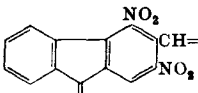
TABLE XIV—Continued
CONDENSATIONS WITH AROMATIC NITRO COMPOUNDS

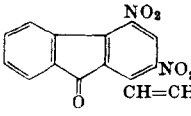
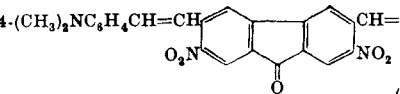
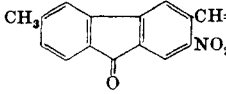
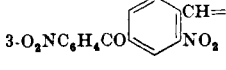
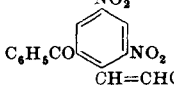
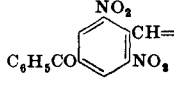
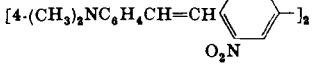
B. <i>Aromatic Aldehydes—Continued</i>					
Aldehyde or Ketone	Nitro Compound	Catalyst	Temperature	Product(s) and Yield(s) (%)	Refs.
Benzaldehyde (contd.)	4-O ₂ N-2-C ₆ H ₄ -NHO ₂ SC ₆ H ₃ CH ₃	Piperidine	150-160°	C ₆ H ₅ CH=CHC ₆ H ₃ NO ₂ -4-SO ₂ NHC ₆ H ₃ -2 (45)	218
	2,4,6-(O ₂ N) ₃ -C ₆ H ₂ CH ₃	"	Boiling C ₆ H ₆ or water bath	C ₆ H ₅ CH=CHC ₆ H ₂ (NO ₂) ₃ -2,4,6 (80)	218, 1064, 1066
	3-O ₂ N-6-HOCH ₂ -CH ₂ O ₂ SC ₆ H ₃ CH ₃	"	140°	C ₆ H ₅ CH=CHC ₆ H ₃ NO ₂ -3-SO ₂ CH ₂ CH ₂ OH-6 (54)	1068
	2-Nitro-3-methylfluorenone	"	150°	 (76)	1069
	2,7-Dinitro-3-methylfluorenone	"	130°	 (86)	1069
	2,4-Dinitro-1-methylfluorenone	"	145°	 (40)	1069
	2,4-Dinitro-3-methylfluorenone	"	150°	 (81)	1069

	2,7-Dinitro-3,6-dimethylfluorenone	"	150°		(91) 1069
	2-Nitro-3,6-dimethylfluorenone	"	150°		(94) 1069
	3-Nitro-4,4'-dimethylbenzo-phenone	"	150-155°	2-O ₂ N-4-(4'-CH ₃ C ₆ H ₄ CO)C ₆ H ₃ CH=CHC ₆ H ₅	(43) 1069
Salicylaldehyde	4-O ₂ NC ₆ H ₄ -CH ₃ CO ₂ C ₆ H ₅	CH ₃ CO ₂ NH ₄	Boiling C ₂ H ₅ OH		(98) 217
4-Hydroxy-benzaldehyde	2,4-(O ₂ N) ₂ C ₆ H ₃ CH ₃	Piperidine	155°	4-HOC ₆ H ₄ CH=CHC ₆ H ₃ (NO ₂) ₂ -2,4	(—) 1065
	2,6-(O ₂ N) ₂ C ₆ H ₃ CH ₃	"	140°	4-HOC ₆ H ₄ CH=CHC ₆ H ₃ (NO ₂) ₂ -2,6	(92) 1067
3,4-Methylenedioxy-benzaldehyde	2-O ₂ N-4-NCC ₆ H ₃ CH ₃	"	150°	3,4-CH ₂ O ₂ C ₆ H ₃ CH=CHC ₆ H ₃ NO ₂ -2-CN-4	(70) 1062
(piperonal)	2,4-(O ₂ N) ₂ C ₆ H ₃ CH ₃	"	150-160°	3,4-CH ₂ O ₂ C ₆ H ₃ CH=CHC ₆ H ₃ (NO ₂) ₂ -2,4	(—) 243
4-Methylbenzaldehyde	4-O ₂ NC ₆ H ₄ CH ₃ CO ₂ H	"	140°	4-CH ₃ C ₆ H ₄ CH=CHC ₆ H ₄ NO ₂ -4	(13) 1062
	2,4-(O ₂ N) ₂ C ₆ H ₃ CH ₃	"	165°	4-CH ₃ C ₆ H ₄ CH=CHC ₆ H ₃ (NO ₂) ₂ -2,4	(65) 1065
	2-O ₂ N-4-NCC ₆ H ₃ CH ₃	"	160°	4-CH ₃ C ₆ H ₄ CH=CHC ₆ H ₃ NO ₂ -2-CN-4	(50) 1065
2-Methoxy-benzaldehyde	4-O ₂ NC ₆ H ₄ CH ₃ CO ₂ H	"	120°	2-CH ₃ OC ₆ H ₄ CH=CHC ₆ H ₄ NO ₂ -4	(40) 1062
	2-O ₂ N-4-NCC ₆ H ₃ CH ₃	"	100°	2-CH ₃ OC ₆ H ₄ CH=CHC ₆ H ₃ NO ₂ -2-CN-4	(80) 1062
3-Methoxy-benzaldehyde	4-O ₂ NC ₆ H ₄ CH ₃ CO ₂ H	"	160°	3-CH ₃ OC ₆ H ₄ CH=CHC ₆ H ₄ NO ₂ -4	(—) 1062
4-Methoxybenzaldehyde (anisaldehyde)	4-O ₂ NC ₆ H ₄ CH ₃ CO ₂ H	"	130°	4-CH ₃ OC ₆ H ₄ CH=CHC ₆ H ₄ NO ₂ -4	(50) 1062
	"	CH ₃ CO ₂ NH ₄	Boiling CH ₃ CO ₂ H	4-CH ₃ OC ₆ H ₄ CH=C(CO ₂ H)C ₆ H ₄ NO ₂ -4	(5) 217
				4-CH ₃ OC ₆ H ₄ CH=CHC ₆ H ₄ NO ₂ -4	(6)

Note: References 285 to 1153 are on pp. 582-599.

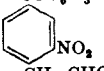
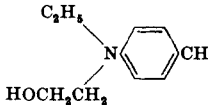
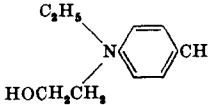
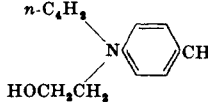
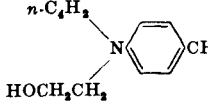
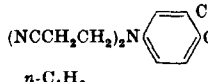
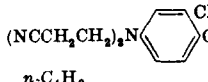
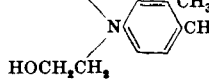
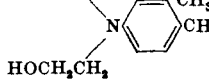
TABLE XIV—Continued
CONDENSATIONS WITH AROMATIC NITRO COMPOUNDS

B. Aromatic Aldehydes—Continued					
Aldehyde	Nitro Compound	Catalyst	Temperature	Product(s) and Yield(s) (%)	Refs.
4-Methoxybenzaldehyde (anisaldehyde) (contd.)	2,4-(O ₂ N) ₂ C ₆ H ₃ CH ₃	Piperidine	180°	4-CH ₃ OC ₆ H ₄ CH=CHC ₆ H ₃ (NO ₂) ₂ -2,4	(67) 1065
	4-O ₂ N-2-NCC ₆ H ₃ CH ₃	"	140-150°	4-CH ₃ OC ₆ H ₄ CH=CHC ₆ H ₃ NO ₂ -4-CN-2	(—) 1062
	2,4,6-(O ₂ N) ₃ C ₆ H ₂ CH ₃	"	Water bath	4-CH ₃ OC ₆ H ₄ CH=CHC ₆ H ₂ (NO ₂) ₃ -2,4,6	(—) 1062
	2-O ₂ N-4,5-(CH ₃ O) ₂ -C ₆ H ₃ CH ₂ CN	"	Boiling C ₂ H ₅ OH	4-CH ₃ OC ₆ H ₄ CH=C(CN)C ₆ H ₃ NO ₂ -2-(OCH ₃) ₂ -4,5	(—) 1070
3-Methoxy-4-hydroxy-benzaldehyde (vanillin)	2,4-(O ₂ N) ₂ C ₆ H ₃ CH ₃	"	150-160°	4-HO-3-CH ₃ OC ₆ H ₃ CH=CHC ₆ H ₃ (NO ₂) ₂ -2,4	(20) 243
	2,6-(O ₂ N) ₂ C ₆ H ₃ CH ₃	"	130°	4-HO-3-CH ₃ OC ₆ H ₃ CH=CHC ₆ H ₃ (NO ₂) ₂ -2,6	(93) 1067
4-Dimethylamino-benzaldehyde	4-O ₂ NC ₆ H ₄ CH ₂ CO ₂ H	"	116°	4-(CH ₃) ₂ NC ₆ H ₄ CH=CHC ₆ H ₄ NO ₂ -4	(48) 1062, 1071
	2-O ₂ N-4-NCC ₆ H ₃ CH ₃	"	120°	4-(CH ₃) ₂ NC ₆ H ₄ CH=CHC ₆ H ₃ NO ₂ -2-CN-4	(—) 1062
	4-O ₂ N-2-NCC ₆ H ₃ CH ₃	"	120-130°	4-(CH ₃) ₂ NC ₆ H ₄ CH=CHC ₆ H ₃ NO ₂ -4-CN-2	(35) 1062
	2-Nitro-3-methyl-fluorenone	"	150°		CH=CHC ₆ H ₄ N(CH ₃) ₂ -4 (81) 1069
	2,7-Dinitro-3-methylfluorenone	"	105°		CH=CHC ₆ H ₄ N(CH ₃) ₂ (94) 1069
	2,4-Dinitro-3-methylfluorenone	"	150°		CH=CHC ₆ H ₄ N(CH ₃) ₂ -4 (91) 1069

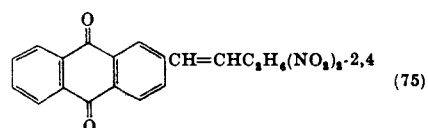
2,4-Dinitro-1-methylfluorenone	..	Water bath		(55)	1069
2,7-Dinitro-3,6-dimethylfluorenone	..	125°		(89)	1069
2-Nitro-3,6-dimethylfluorenone	..	130°		(94)	1069
3,3'-Dinitro-4-methylbenzophenone	..	145-150°		(75)	1069
3,5-Dinitro-2-methylbenzophenone	..	120°		(75)	1069
3,5-Dinitro-4-methylbenzophenone	..	Water bath		(45)	1069
3,3'-Dinitro-4,4'-dimethylbenzophenone	..	150-155°		(70)	1069

Note: References 285 to 1153 are on pp. 582-599.

TABLE XIV—Continued
CONDENSATIONS WITH AROMATIC NITRO COMPOUNDS

B. Aromatic Aldehydes—Continued					
Aldehyde	Nitro Compound	Catalyst	Temperature	Product(s) and Yield(s) (%)	Refs.
4-Dimethylamino-benzaldehyde (contd.)	3-Nitro-4,4'-dimethylbenzophenone	..	135-140°	 COC ₆ H ₃ NO ₂ -3-CH ₃ -4 (52)	1069
1-Naphthaldehyde	2,4-(O ₂ N) ₂ C ₆ H ₃ CH ₃	..	130-140°	1-C ₁₀ H ₇ CH=CHC ₆ H ₃ (NO ₂) ₂ -2,4 (95)	500
4-Diethylamino-benzaldehyde	2,4-(O ₂ N) ₂ C ₆ H ₃ CH ₃	..	Heat	4-(C ₂ H ₅) ₂ NC ₆ H ₄ CH=CHC ₆ H ₃ (NO ₂) ₂ -2,4 (Low)	1071
	2,4-(O ₂ N) ₂ C ₆ H ₃ CH ₃	 CH=CHC ₆ H ₄ (NO ₂) ₂ -2,4 (Quant.)	1071
4-N,N-Di(2'-cyanoethyl)amino-benzaldehyde	2,4-(O ₂ N) ₂ C ₆ H ₃ CH ₃	4-(NCCH ₂ CH ₂) ₂ NC ₆ H ₄ CH=CHC ₆ H ₃ (NO ₂) ₂ -2,4 (—)	533
	2,4-(O ₂ N) ₂ C ₆ H ₃ CH ₃	 CH=CHC ₆ H ₃ (NO ₂) ₂ -2,4 (Good)	1071
(NCCH ₂ CH ₂) ₂ N 	2,4-(O ₂ N) ₂ C ₆ H ₃ CH ₃	 CH=CHC ₆ H ₃ (NO ₂) ₂ -2,4 (—)	533
	2,4-(O ₂ N) ₂ C ₆ H ₃ CH ₃	 CH=CHC ₆ H ₃ (NO ₂) ₂ -2,4 (Fair)	1071

Anthraquinone-3-carboxaldehyde 2,4-(O₂N)₂C₆H₃CH₃ Piperidine/C₆H₅NO₂ 140°



C. Heterocyclic Aldehydes

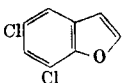
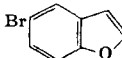
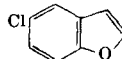
5-Chlorothiophene-2-carboxaldehyde	2,4,6-(O ₂ N) ₃ C ₆ H ₂ CH ₃	Piperidine	Boiling C ₆ H ₆	CH=CHC ₆ H ₂ (NO ₂) ₃ -2,4,6 (—)	958
Furfural	4-O ₂ NC ₆ H ₄ CH ₂ CO ₂ H	„	130–140°	2-C ₆ H ₄ OCH=CHC ₆ H ₄ NO ₂ -4 (15)	1072
Thiophene-2-carboxaldehyde	2,4,6-(O ₂ N) ₃ C ₆ H ₂ CH ₃	„	Boiling xylene or benzene	2-C ₆ H ₄ SCH=CHC ₆ H ₂ (NO ₂) ₃ -2,4,6 (85)	775, 958
5-Methylthiophene-2-carboxaldehyde	2,4,6-(O ₂ N) ₃ C ₆ H ₂ CH ₃	„	Boiling C ₆ H ₆	CH=CHC ₆ H ₂ (NO ₂) ₃ -2,4,6 (—)	958
2,5-Dimethylthiophene-3-carboxaldehyde	2,4,6-(O ₂ N) ₃ C ₆ H ₂ CH ₃	„	„	CH=CHC ₆ H ₂ (NO ₂) ₃ -2,4,6 (—)	958
Quinoline-6-carboxaldehyde	4-O ₂ NC ₆ H ₄ CH ₂ CO ₂ H	„	130–140°	6-C ₁₀ H ₇ NCH=CHC ₆ H ₄ NO ₂ -4 (30)	1072
Quinoline-8-carboxaldehyde	4-O ₂ NC ₆ H ₄ CH ₂ CO ₂ H	„	„	8-C ₁₀ H ₇ NCH=CHC ₆ H ₄ NO ₂ -4 (25)	1072

Note: References 285 to 1153 are on pp. 582–599.

TABLE XV
CONDENSATIONS WITH ALKYL AND ARYL SULFONYL COMPOUNDS

524

ORGANIC REACTIONS

A. Acyclic Aldehydes					
Aldehyde	Sulfonyl Compound	Catalyst	Temperature	Product(s) and Yield(s) (%)	Refs.
Formaldehyde	$C_6H_5SO_2CH(C_2H_5)CO_2H$	$(CH_3)_2NH$	0°, then room	$C_6H_5SO_2C(C_2H_5)=CH_2$ (44)	219
	$C_6H_5SO_2CH(C_3H_7-i)CO_2H$	"	"	$C_6H_5SO_2C(C_3H_7-i)=CH_2$ (43)	219
	$C_6H_5SO_2CH(C_4H_9-n)CO_2H$	"	"	$C_6H_5SO_2C(C_4H_9-n)=CH_2$ (9)	219
	$C_6H_5SO_2CH(CH_2C_6H_5)CO_2H$	"	"	$C_6H_5SO_2C(CH_2C_6H_5)=CH_2$ (65)	219
Chloral	$n-C_4H_9SO_2CH_2CO_2C_2H_5$	$CH_3CO_2NH_4$	Boiling C_6H_6	$n-C_4H_9SO_2C(CO_2C_2H_5)=CHCCl_3$ (61)	219
n-Butyraldehyde	$n-C_4H_9SO_2CH_2CO_2C_2H_5$	Piperidinium acetate	"	$n-C_4H_9SO_2C(CO_2C_2H_5)=CHC_3H_7-n$ (77)	219
Isobutyraldehyde	$n-C_4H_9SO_2CH_2CO_2C_2H_5$	"	"	$n-C_4H_9SO_2C(CO_2C_2H_5)=CHC_3H_7-i$ (88)	219
n-Octanal	$CH_2(SO_2C_2H_5)_2$	"	Boiling $C_6H_5CH_3$	$(C_2H_5O_2S)_2C=CHC_7H_{15}-n$ (38)	221
B. Aromatic Aldehydes					
Cinnamaldehyde	$n-C_4H_9SO_2CH_2CO_2C_2H_5$	"	Boiling C_6H_6	$n-C_4H_9SO_2C(CO_2C_2H_5)=CHCH=CHC_6H_5$ (84)	219
	$HO_2CCH_2SO_2CH_2CO_2H$	"	"	$SO_2[C(CO_2H)=CHCH=CHC_6H_5]_2$ (53)	1073
	$C_2H_5O_2CCH_2SO_2CH_2CO_2C_2H_5$	"	"	$SO_2[C(CO_2C_2H_5)=CHCH=CHC_6H_5]_2$ (47)	1073
	$C_6H_5SO_2CH_2CO_2C_2H_5$	$CH_3CO_2NH_4$	Room	$C_6H_5SO_2C(CO_2C_2H_5)=CHCH=CHC_6H_5$ (70)	1076
	$4-CH_3C_6H_4SO_2CH_2CO_2H$	Piperidine + pyridine	Water bath	$4-CH_3C_6H_4SO_2CH=CHCH=CHC_6H_5$ (50)	219
4-Dimethylamino-cinnamaldehyde	$4-CH_3C_6H_4SO_2CH_2-C_6H_3(NO_2)_2-2,4$	Piperidinium acetate	Boiling C_6H_6	$4-CH_3C_6H_4SO_2CC_6H_3(NO_2)_2-2,4$ $ $ $CHCH=CHC_6H_4N(CH_3)_2-4$ (—)	760
C. Aromatic Aldehydes					
2,4,6-Trichlorobenzaldehyde	$4-ClC_6H_4SO_2CH_2CO_2H$	$C_6H_5CH_2NH_2$	Boiling CH_3CO_2H	$4-ClC_6H_4SO_2CH=CHC_6H_2Cl_3-2,4,6$ (28)	1074
3,5-Dibromosalicylaldehyde	$4-CH_3CONHC_6H_4SO_2-CH_2COC_6H_5$	Piperidine	100°	$4-CH_3CONHC_6H_4SO_2CCOC_6H_5$ $ $ $CHC_6H_3OH-2-Br_2-3,5$ (76)	1075
	$4-CH_3CONHC_6H_4SO_2CH_2-C_6H_4NHCOC_6H_3-4$	"	"	$4-CH_3CONHC_6H_4SO_2CC_6H_4NHCOC_6H_3-4$ $ $ $CHC_6H_3OH-2-Br_2-3,5$ (83)	1075
3,4-Dichlorobenzaldehyde	$CH_2(SO_2C_2H_5)_2$	Piperidinium acetate	Boiling $C_6H_5CH_3$	$(C_2H_5O_2S)_2C=CC_6H_3Cl_2-3,4$ (16)	221
3,5-Dichlorosalicylaldehyde	$CH_2(SO_2C_2H_5)_2$	Piperidine or $(C_2H_5)_3N$	"	 $SO_2C_2H_5$ (62)	221
5-Bromosalicylaldehyde	$CH_2(SO_2C_2H_5)_2$	"	"	 $SO_2C_2H_5$ (39)	221
2-Chlorobenzaldehyde	$n-C_4H_9SO_2CH_2CO_2C_2H_5$	Piperidinium acetate	Boiling C_6H_6	$n-C_4H_9SO_2C(CO_2C_2H_5)=CHC_6H_4Cl-2$ (71)	219
	$C_6H_5SO_2CH_2CN$	$CH_3CO_2NH_4$	Cold, then boiling C_2H_5OH	$C_6H_5SO_2C(CN)=CHC_6H_4Cl-2$ (98)	1076
4-Chlorobenzaldehyde	$C_6H_5SO_2CH_2CO_2H$	"	Boiling CH_3CO_2H	$C_6H_5SO_2CH=CHC_6H_4Cl-4$ (28)	220
	$C_6H_5SO_2CH_2CN$	"	Cold, then boiling C_2H_5OH	$C_6H_5SO_2CH_2CH(NH_2)C_6H_4Cl-4$ (24)	1076
	$4-CH_3C_6H_4SO_2CH_2CO_2H$	"	Boiling CH_3CO_2H	$C_6H_5SO_2C(CN)=CHC_6H_4Cl-4$ (95)	1076
	$4-CH_3C_6H_4SO_2CH_2CO_2H$	"	Boiling CH_3CO_2H	$4-CH_3C_6H_4SO_2CH=CHC_6H_4Cl-4$ (31)	220
	$4-CH_3C_6H_4SO_2CH_2CH(NH_2)C_6H_4Cl-4$	"	Boiling CH_3CO_2H	$4-CH_3C_6H_4SO_2CH_2CH(NH_2)C_6H_4Cl-4$ (19)	220
	$4-ClC_6H_4SO_2CH_2CO_2H$	$C_6H_5CH_2NH_2$	Boiling CH_3CO_2H	$4-ClC_6H_4SO_2CH=CHC_6H_4Cl-4$ (22)	1074
	$2,4,5-Cl_3C_6H_2SO_2-CH_2CO_2C_2H_5$	"	"	$2,4,5-Cl_3C_6H_2SO_2-CH_2CO_2C_2H_5$ $ $ $C(CO_2C_2H_5)=CHC_6H_4Cl-4$ (44)	1074
5-Chlorosalicylaldehyde	$CH_2(SO_2C_2H_5)_2$	Piperidine or $(C_2H_5)_3N$	Boiling $C_6H_5CH_3$	 $SO_2C_2H_5$ (54)	221
2-Nitrobenzaldehyde	$C_6H_5SO_2CH_2CO_2H$	$CH_3CO_2NH_4$	Boiling CH_3CO_2H	$C_6H_5SO_2CH=CHC_6H_4NO_2-2$ (9)	220
	$C_6H_5SO_2CH_2CN$	"	Cold, then boiling C_2H_5OH	$C_6H_5SO_2CH_2CH(NH_2)C_6H_4NO_2-2$ (7)	1076
	$4-CH_3C_6H_4SO_2CH_2CO_2H$	"	Boiling CH_3CO_2H	$C_6H_5SO_2C(CN)=CHC_6H_4NO_2-2$ (93)	1076
	$4-CH_3C_6H_4SO_2CH_2CO_2H$	"	Boiling CH_3CO_2H	$4-CH_3C_6H_4SO_2CH=CHC_6H_4NO_2-2$ (31)	220
	$4-CH_3C_6H_4SO_2CH_2CH(NH_2)C_6H_4NO_2-2$	"	Boiling CH_3CO_2H	$4-CH_3C_6H_4SO_2CH_2CH(NH_2)C_6H_4NO_2-2$ (19)	220
3-Nitrobenzaldehyde	$C_6H_5SO_2CH_2CO_2H$	"	Boiling CH_3CO_2H	$C_6H_5SO_2CH=CHC_6H_4NO_2-3$ (14)	220
	$C_6H_5SO_2CH_2CO_2C_2H_5$	"	Room	$C_6H_5SO_2CH_2CH(NH_2)C_6H_4NO_2-3$ (21)	1076
	$C_6H_5SO_2CH_2COC_6H_5$	"	Cold, then boiling C_2H_5OH	$C_6H_5SO_2C(CO_2C_2H_5)=CHC_6H_4NO_2-3$ (70)	1076
		"		$C_6H_5SO_2C(COC_6H_5)=CHC_6H_4NO_2-3$ (48)	1076

Note: References 285 to 1153 are on pp. 582-599.

THE KNOEVENAGEL CONDENSATION

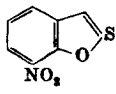
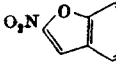
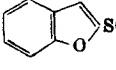
525

TABLE XV—Continued
CONDENSATIONS WITH ALKYL AND ARYL SULFONYL COMPOUNDS

526

ORGANIC REACTIONS

THE KNOEVENAGEL CONDENSATION

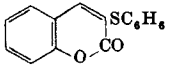
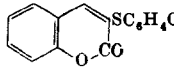
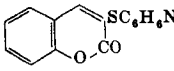
C. Aromatic Aldehydes—Continued					
Aldehyde	Sulfonyl Compound	Catalyst	Temperature	Product(s) and Yield(s) (%)	Refs.
3-Nitrobenzaldehyde (<i>contd.</i>)	4-CH ₃ C ₆ H ₄ SO ₂ CH ₂ CO ₂ H	CH ₃ CO ₂ NH ₄	Boiling CH ₃ CO ₂ H	4-CH ₃ C ₆ H ₄ SO ₂ CH=CHC ₆ H ₃ (NO ₂) ₃ (20)	220
	4-CH ₃ C ₆ H ₄ SO ₂ CH(CH ₃)CO ₂ H	"	"	4-CH ₃ C ₆ H ₄ SO ₂ CH(CH ₃)CH(NH ₂)C ₆ H ₃ (NO ₂) ₃ * (25)	220
				4-CH ₃ C ₆ H ₄ SO ₂ C(CH ₃)=CHC ₆ H ₃ (NO ₂) ₃ (10)	220
4-Nitrobenzaldehyde	CH ₃ (SO ₂ C ₆ H ₅) ₂	Piperidinium acetate	Boiling C ₆ H ₅ CH ₃	(C ₆ H ₄ O ₂ S) ₂ C=CC ₆ H ₄ NO ₂ -4 (48)	221
3-Nitrosalicylaldehyde	CH ₃ (SO ₂ C ₆ H ₄) ₂	Piperidine or (C ₂ H ₅) ₃ N	"	 (25)	221
5-Nitrosalicylaldehyde	CH ₃ (SO ₂ C ₆ H ₄) ₂	"	"	 (22)	221
Benzaldehyde	n-C ₄ H ₉ SO ₂ CH ₂ CO ₂ C ₂ H ₅	Piperidinium acetate	Boiling C ₆ H ₆	n-C ₄ H ₉ SO ₂ C(CO ₂ C ₂ H ₅)=CHC ₆ H ₅ (83)	219
	SO ₂ (CH ₂ CO ₂ H) ₂	"	"	C ₆ H ₅ CH=CHSO ₂ CH=CHC ₆ H ₅ (60)	1073
	CH ₃ (SO ₂ C ₆ H ₅) ₂	"	Boiling C ₆ H ₅ CH ₃	C ₆ H ₅ CH=C(SO ₂ C ₆ H ₅) ₂ (29)	221
	SO ₂ (CH ₂ CO ₂ C ₂ H ₅) ₂	"	Boiling C ₆ H ₆	SO ₂ [C(CO ₂ C ₂ H ₅)=CHC ₆ H ₅] ₂ (39)	1073
	C ₆ H ₅ SO ₂ CH ₂ CO ₂ H	CH ₃ CO ₂ NH ₄	Boiling CH ₃ CO ₂ H	C ₆ H ₅ SO ₂ CH=CHC ₆ H ₅ (21)	220
	"	C ₆ H ₅ CH ₂ NH ₂	"	C ₆ H ₅ SO ₂ CH ₂ CH(NH ₂)C ₆ H ₅ (27)	220
	"	"	"	C ₆ H ₅ SO ₂ CH=CHC ₆ H ₅ (27)	220
	C ₆ H ₅ SO ₂ CH ₂ CN	CH ₃ CO ₂ NH ₄	Cold, then boiling C ₂ H ₅ OH	C ₆ H ₅ SO ₂ CH ₂ CH(NHCH ₂ C ₆ H ₅)C ₆ H ₅ (10)	1076
	4-CH ₃ C ₆ H ₄ SO ₂ CH ₂ CO ₂ H	Piperidine + pyridine	Water bath	4-CH ₃ C ₆ H ₄ SO ₂ CH=CHC ₆ H ₅ (18)	219
	"	CH ₃ CO ₂ NH ₄	Boiling CH ₃ CO ₂ H	4-CH ₃ C ₆ H ₄ SO ₂ CH=CHC ₆ H ₅ (25)	220
	4-CH ₃ C ₆ H ₄ SO ₂ CH(CH ₃)CO ₂ H	"	"	4-CH ₃ C ₆ H ₄ SO ₂ CH ₂ CH(NH ₂)C ₆ H ₅ (23)* 4-CH ₃ C ₆ H ₄ SO ₂ C(CH ₃)=CHC ₆ H ₅ (12) 4-CH ₃ C ₆ H ₄ SO ₂ CH(CH ₃)CH(NH ₂)C ₆ H ₅ (16)	220
Salicylaldehyde	4-CH ₃ CONHC ₆ H ₄ SO ₂ -CH ₂ COC ₆ H ₅	Piperidine + pyridine	100°	4-CH ₃ CONHC ₆ H ₄ SO ₂ CCOC ₆ H ₅ (96)	1075
	4-CH ₃ CONHC ₆ H ₄ SO ₂ CH ₂ -COC ₆ H ₄ NHCOCH ₃ -4	"	100°	4-CH ₃ CONHC ₆ H ₄ SO ₂ CCOC ₆ H ₄ NHCOCH ₃ -4 (83)	1075
	CH ₃ (SO ₂ C ₆ H ₅) ₂	Piperidine or (C ₂ H ₅) ₃ N	Boiling C ₆ H ₅ CH ₃	 (59)	221
3,4-Methylenedioxybenzaldehyde (piperonal)	C ₆ H ₃ SO ₂ CH ₂ CO ₂ H	CH ₃ CO ₂ NH ₄	Boiling CH ₃ CO ₂ H	C ₆ H ₃ SO ₂ CH=CHC ₆ H ₃ O ₂ CH ₂ -3,4 (19)	220
	C ₆ H ₃ SO ₂ CH ₂ CN	CH ₃ CO ₂ NH ₄	Room, then boiling C ₆ H ₅ OH	C ₆ H ₃ SO ₂ CH ₂ CH(NH ₂)C ₆ H ₃ O ₂ CH ₂ -3,4 (30)	1076
	C ₆ H ₃ SO ₂ CH ₂ COC ₆ H ₅	"	"	C ₆ H ₃ SO ₂ C(CO ₂ C ₆ H ₅)=CHC ₆ H ₃ O ₂ CH ₂ -3,4 (17)	1076
	4-CH ₃ C ₆ H ₄ SO ₂ CH ₂ CO ₂ H	"	Boiling CH ₃ CO ₂ H	4-CH ₃ C ₆ H ₄ SO ₂ CH=CHC ₆ H ₃ O ₂ CH ₂ -3,4 (15)	220
	"	C ₆ H ₅ CH ₂ NH ₂	"	4-CH ₃ C ₆ H ₄ SO ₂ CH ₂ CH(NH ₂)C ₆ H ₃ O ₂ CH ₂ -3,4 (22) 4-CH ₃ C ₆ H ₄ SO ₂ CH=CHC ₆ H ₃ O ₂ CH ₂ -3,4 (30) 4-CH ₃ C ₆ H ₄ SO ₂ CH ₂ CH(NHCH ₂ C ₆ H ₅)C ₆ H ₃ O ₂ CH ₂ -3,4 (27)	220
4-Methylbenzaldehyde	C ₆ H ₃ SO ₂ CH ₂ CO ₂ H	CH ₃ CO ₂ NH ₄	"	C ₆ H ₃ SO ₂ CH=CHC ₆ H ₃ CH ₃ -4 (17)	220
	C ₆ H ₃ SO ₂ CH ₂ CN	"	Cold, then boiling C ₆ H ₅ OH	C ₆ H ₃ SO ₂ C(CN)=CHC ₆ H ₃ CH ₃ -4 (62)	1076
	C ₆ H ₃ SO ₂ CH ₂ COC ₆ H ₅	"	"	C ₆ H ₃ SO ₂ C(CO ₂ C ₆ H ₅)=CHC ₆ H ₃ CH ₃ -4 (68)	1076
2-Methoxybenzaldehyde	4-CH ₃ C ₆ H ₄ SO ₂ CH ₂ CO ₂ H	"	Boiling CH ₃ CO ₂ H	4-CH ₃ C ₆ H ₄ SO ₂ CH=CHC ₆ H ₃ CH ₃ -4 (22)	220
	C ₆ H ₃ SO ₂ CH ₂ CO ₂ H	"	"	4-CH ₃ C ₆ H ₄ SO ₂ CH ₂ CH(NH ₂)C ₆ H ₃ CH ₃ -4 (25)	220
	C ₆ H ₃ SO ₂ CH ₂ CN	"	"	C ₆ H ₃ SO ₂ CH=CHC ₆ H ₃ OCH ₃ -2 (28)	220
	C ₆ H ₃ SO ₂ CH ₂ COC ₆ H ₅	"	Cold, then boiling C ₂ H ₅ OH	C ₆ H ₃ SO ₂ CH ₂ CH(NH ₂)C ₆ H ₃ OCH ₃ -2 (20)	1076
	4-CH ₃ C ₆ H ₄ SO ₂ CH ₂ CO ₂ H	"	Boiling CH ₃ CO ₂ H	C ₆ H ₃ SO ₂ C(CO ₂ C ₆ H ₅)=CHC ₆ H ₃ OCH ₃ -2 (28) 4-CH ₃ C ₆ H ₄ SO ₂ CH=CHC ₆ H ₃ OCH ₃ -2 (23) 4-CH ₃ C ₆ H ₄ SO ₂ CH ₂ CH(NH ₂)C ₆ H ₃ OCH ₃ -2 (19)	220

Note: References 285 to 1153 are on pp. 582-599.

* By using primary amines as catalysts a number of compounds of the general type 4-CH₃C₆H₄SO₂CH₂CH(NHR)C₆H₃(NO₂)₃ were obtained.

527

TABLE XVI
CONDENSATIONS WITH ALKYL AND ARYL SULFIDES

A. Aromatic Aldehydes					
Aldehyde	Sulfide	Catalyst	Temperature	Product(s) and Yield(s) (%)	Refs.
3,4-Dichlorobenzaldehyde	4-O ₂ NC ₆ H ₄ SC ₂ H ₄ CO ₂ H	Piperidine + CH ₃ CO ₂ NH ₄	Boiling CH ₃ CO ₂ H	4-O ₂ NC ₆ H ₄ SC(CO ₂ H)=CHC ₆ H ₃ Cl ₂ -3,4 (49)	1078
2-Chlorobenzaldehyde	4-O ₂ NC ₆ H ₄ SC ₂ H ₄ CO ₂ H	"	"	4-O ₂ NC ₆ H ₄ SC(CO ₂ H)=CHC ₆ H ₄ Cl-2 (54)	1078
4-Chlorobenzaldehyde	4-CH ₃ C ₆ H ₄ SC ₂ H ₄ CO ₂ H	CH ₃ CO ₂ NH ₄	"	4-CH ₃ C ₆ H ₄ SC(CO ₂ H)=CHC ₆ H ₄ Cl-4 (20)	1079
	4-O ₂ NC ₆ H ₄ SC ₂ H ₄ CO ₂ H	Piperidine + CH ₃ CO ₂ NH ₄	"	4-O ₂ NC ₆ H ₄ SC(CO ₂ H)=CHC ₆ H ₄ Cl-4 (62)	1078
2-Nitrobenzaldehyde	4-O ₂ NC ₆ H ₄ SC ₂ H ₄ CO ₂ H	"	"	4-O ₂ NC ₆ H ₄ SC(CO ₂ H)=CHC ₆ H ₄ NO ₂ -2 (14)	1078
3-Nitrobenzaldehyde	4-O ₂ NC ₆ H ₄ SC ₂ H ₄ CO ₂ H	"	"	4-O ₂ NC ₆ H ₄ SC(CO ₂ H)=CHC ₆ H ₄ NO ₂ -3 (30)	1078
4-Nitrobenzaldehyde	4-O ₂ NC ₆ H ₄ SC ₂ H ₄ CO ₂ H	"	"	4-O ₂ NC ₆ H ₄ SC(CO ₂ H)=CHC ₆ H ₄ NO ₂ -4 (32)	1078
Benzaldehyde	C ₆ H ₅ SC ₂ H ₄ CO ₂ H	"	"	C ₆ H ₅ SC(CO ₂ H)=CHC ₆ H ₅ (10)	1079, 1080
	4-CH ₃ C ₆ H ₄ SC ₂ H ₄ CO ₂ H	CH ₃ CO ₂ NH ₄	"	4-CH ₃ C ₆ H ₄ SC(CO ₂ H)=CHC ₆ H ₅ (13)	1079
	4-CH ₃ C ₆ H ₄ SC ₂ H ₄ CONH ₂	Piperidine + CH ₃ CO ₂ NH ₄	"	4-CH ₃ C ₆ H ₄ SC(CONH ₂)=CHC ₆ H ₅ (15)	1079
	4-O ₂ NC ₆ H ₄ SC ₂ H ₄ CO ₂ H (C ₆ H ₅ COCH ₂) ₂ S	"	"	4-O ₂ NC ₆ H ₄ SC(CO ₂ H)=CHC ₆ H ₅ (48)	1078
		Piperidine/alcohol	Room	S[CH(COC ₆ H ₅)CH(C ₆ H ₅)NC ₆ H ₁₀] ₂ (—)	21
Salicylaldehyde	C ₆ H ₅ SC ₂ H ₄ CO ₂ H	CH ₃ CO ₂ NH ₄	Boiling CH ₃ CO ₂ H	 (6)	1079
	4-CH ₃ C ₆ H ₄ SC ₂ H ₄ CO ₂ H	"	"	 (9)	1079
	4-O ₂ NC ₆ H ₄ SC ₂ H ₄ CO ₂ H	Piperidine + CH ₃ CO ₂ NH ₄	"	 (20)	1078
	(C ₆ H ₅ COCH ₂) ₂ S	Piperidine/alcohol	Room	S[CH(COC ₆ H ₅)CH(C ₆ H ₄ OH-2)NC ₆ H ₁₀] ₂ (—)	21
B. Heterocyclic Aldehyde					
3,4-Methylenedioxybenzaldehyde (piperonal)	C ₆ H ₄ SC ₂ H ₄ CO ₂ H	Piperidine + CH ₃ CO ₂ NH ₄	Boiling CH ₃ CO ₂ H	C ₆ H ₅ SC(CO ₂ H)=CHC ₆ H ₃ O ₂ CH ₂ -3,4 (7)	1079
	4-CH ₃ C ₆ H ₄ SC ₂ H ₄ CO ₂ H	CH ₃ CO ₂ NH ₄	"	4-CH ₃ C ₆ H ₄ SC(CO ₂ H)=CHC ₆ H ₃ O ₂ CH ₂ -3,4 (22)	1079
	4-CH ₃ C ₆ H ₄ SC ₂ H ₄ CONH ₂	"	"	4-CH ₃ C ₆ H ₄ SC(CONH ₂)=CHC ₆ H ₃ O ₂ CH ₂ -3,4 (—)	1079
	4-O ₂ NC ₆ H ₄ SC ₂ H ₄ CO ₂ H	Piperidine + CH ₃ CO ₂ NH ₄	"	4-O ₂ NC ₆ H ₄ SC(CO ₂ H)=CHC ₆ H ₃ O ₂ CH ₂ -3,4 (25)	1078
4-Methylbenzaldehyde	C ₆ H ₅ SC ₂ H ₄ CO ₂ H	"	"	C ₆ H ₅ SC(CO ₂ H)=CHC ₆ H ₄ CH ₃ -4 (11)	1079
	4-CH ₃ C ₆ H ₄ SC ₂ H ₄ CO ₂ H	CH ₃ CO ₂ NH ₄	"	4-CH ₃ C ₆ H ₄ SC(CO ₂ H)=CHC ₆ H ₄ CH ₃ -4 (19)	1079
	4-O ₂ NC ₆ H ₄ SC ₂ H ₄ CO ₂ H	Piperidine + CH ₃ CO ₂ NH ₄	"	4-O ₂ NC ₆ H ₄ SC(CO ₂ H)=CHC ₆ H ₄ CH ₃ -4 (24)	1078
2-Methoxybenzaldehyde	4-CH ₃ C ₆ H ₄ SC ₂ H ₄ CO ₂ H	CH ₃ CO ₂ NH ₄	"	4-CH ₃ C ₆ H ₄ SC(CO ₂ H)=CHC ₆ H ₄ OCH ₃ -2 (16)	1079
	4-O ₂ NC ₆ H ₄ SC ₂ H ₄ CO ₂ H	Piperidine + CH ₃ CO ₂ NH ₄	"	4-O ₂ NC ₆ H ₄ SC(CO ₂ H)=CHC ₆ H ₄ OCH ₃ -2 (50)	1078
4-Methoxybenzaldehyde (anisaldehyde)	C ₆ H ₅ SC ₂ H ₄ CO ₂ H	"	"	C ₆ H ₅ SC(CO ₂ H)=CHC ₆ H ₄ OCH ₃ -4 (7)	1079
	4-CH ₃ C ₆ H ₄ SC ₂ H ₄ CO ₂ H	CH ₃ CO ₂ NH ₄	"	4-CH ₃ C ₆ H ₄ SC(CO ₂ H)=CHC ₆ H ₄ OCH ₃ -4 (20)	1079
	4-O ₂ NC ₆ H ₄ SC ₂ H ₄ CO ₂ H	Piperidine + CH ₃ CO ₂ NH ₄	"	4-O ₂ NC ₆ H ₄ SC(CO ₂ H)=CHC ₆ H ₄ OCH ₃ -4 (33)	1078
	(C ₆ H ₅ COCH ₂) ₂ S	Piperidine/alcohol	Room	4-CH ₃ OC ₆ H ₄ CH=C(COC ₆ H ₅)SCH(COC ₆ H ₅)CH(C ₆ H ₄ OCH ₃ -4)NC ₆ H ₁₀ (—)	21
3,4-Dimethoxybenzaldehyde (veratraldehyde)	4-O ₂ NC ₆ H ₄ SC ₂ H ₄ CO ₂ H	Piperidine + CH ₃ CO ₂ NH ₄	Boiling CH ₃ CO ₂ H	4-O ₂ NC ₆ H ₄ SC(CO ₂ H)=CHC ₆ H ₃ (OCH ₃) ₂ -3,4 (22)	1078
4-Dimethylamino-benzaldehyde	(C ₆ H ₅ COCH ₂) ₂ S	Piperidine/alcohol	Room	4-(CH ₃) ₂ NC ₆ H ₄ CH=C(COC ₆ H ₅)SCH(COC ₆ H ₅)CH(C ₆ H ₄ N(CH ₃) ₂ -4)NC ₆ H ₁₀ (—)	21
1-Naphthaldehyde	4-O ₂ NC ₆ H ₄ SC ₂ H ₄ CO ₂ H	Piperidine + CH ₃ CO ₂ NH ₄	Boiling CH ₃ CO ₂ H	4-O ₂ NC ₆ H ₄ SC(CO ₂ H)=CHC ₁₀ H ₇ -1 (24)	1078
Thiophene-2-carboxaldehyde	4-O ₂ NC ₆ H ₄ SC ₂ H ₄ CO ₂ H	Piperidine + CH ₃ CO ₂ NH ₄	Boiling CH ₃ CO ₂ H	4-O ₂ NC ₆ H ₄ SC(CO ₂ H)=CHC ₄ H ₃ S-2 (38)	1078

Note: References 285 to 1153 are on pp. 582-599.

TABLE XVII
CONDENSATIONS WITH ACTIVE METHYLENE GROUPS ATTACHED TO HETEROCYCLIC SYSTEMS

A. Acyclic Aldehydes or Ketones					
Aldehyde or Ketone	Heterocyclic Compound	Catalyst	Temperature	Product(s) and Yield(s) (%)	Refs.
Formaldehyde (trioxy-methylene)		Piperidine	150–160°	$[2-C_5H_4NCH(CO_2CH_3)]_2CH_2$ (84)*	1081
Chloral		Pyridine	100°	$2-C_3H_2NSCH_2CHOHCCl_3$ (32)	231
		Excess 2-picoline	B.p.	$2-C_5H_4NCH_2CHOHCCl_3$ (43–48)	1082
	„	Pyridinium acetate	Boiling xylene	$2-C_5H_4NCH_2CHOHCCl_3$ (28)	1083
		Pyridine	120°	$4-C_5H_4NCH_2CHOHCCl_3$ (42)	226
	„	None	Boiling $CH_3CO_2-C_8H_{11}$	$4-C_5H_4NCH=CHCO_2H^\dagger$ (23)	1084
		„	Boiling C_6H_6	$4-C_5H_4NCH(CH_2OH)CHOHCCl_3^\ddagger$ (10) $4-C_5H_4NC(CH_2OH)CHOHCCl_3$ (—)	1085
		„	55°	$4-C_5H_4NCH(CH_2OCH_3)CHOHCCl_3$ (46)	1085
		Piperidine	—	 $CH_2CHOHCCl_3$ (—)	223
		Piperidinium acetate	Boiling xylene	$C_2H_5O_2C-CH_2CHOHCCl_3$ (46)	1086
		Pyridine	120°	$3-C_4H_3N_2CH_2CHOHCCl_3$ (85)	226
		„	Steam bath	$4-C_4H_3N_2CH_2CHOHCCl_3$ (35)	233
		„	120°	$2-C_4H_3N_2CH_2CHOHCCl_3$ (43)	226
		„	120°	$4-C_4H_3N_2CH_2CHOHCCl_3$ (73)	226
		„	120°	$2-C_4H_3N_2CH_2CHOHCCl_3$ (48)	226
		Pyridine; or none	Steam bath	$2-C_7H_4NSCH_2CHOHCCl_3$ (80)	232, 234

Note: References 285 to 1153 are on pp. 582–599.

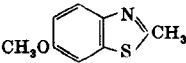
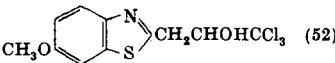
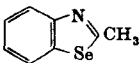
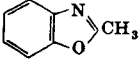
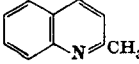
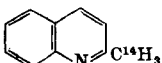
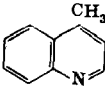
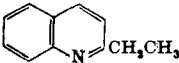
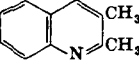
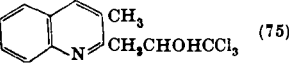
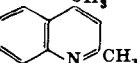

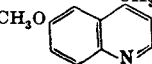
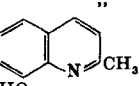
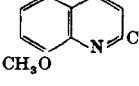
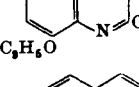
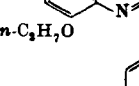
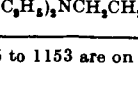
* The yield was calculated on the starting material used.

† The crude product was treated with potassium hydroxide.

‡ The product was hydrolyzed.

TABLE XVII—Continued
CONDENSATIONS WITH ACTIVE METHYLENE GROUPS ATTACHED TO HETEROCYCLIC SYSTEMS

534

A. Acyclic Aldehydes or Ketones—Continued					
Aldehyde or Ketone	Heterocyclic Compound	Catalyst	Temperature	Product(s) and Yield(s) (%)	Refs.
Chloral (<i>contd.</i>)		Pyridine	Steam bath	 (52)	983
		None	„ „	2-C ₇ H ₄ NSeCH ₂ CHOHCCl ₃ (47)	232
		Pyridine	Water bath	2-C ₇ H ₄ NOCH ₂ CHOHCCl ₃ (80)	234
		„	Steam bath	2-C ₈ H ₆ NCH ₂ CHOHCCl ₃ (88)	228, 232, 234, 1087, 1150
		„	Below 100°	2-C ₈ H ₆ NC ¹⁴ H ₉ CH ₂ CHOHCCl ₃ (70)	1088
		„	80–90°; or steam bath	4-C ₈ H ₆ NCH ₂ CHOHCCl ₃ (80)	228, 232, 944
		„	Water bath	2-C ₈ H ₆ NCH(CH ₃)CHOHCCl ₃ (57)	228
		„	Steam bath	 (75)	229
		—	—	 (—)	228
		None	Boiling xylene	6-CH ₃ OC ₈ H ₆ NCH ₂ CHOHCCl ₃ -4 (91)	227
	„	Pyridine	Steam bath	6-CH ₃ OC ₈ H ₆ NCH ₂ CHOHCCl ₃ -4 (78)	1089
		„	„ „	8-HOC ₈ H ₆ NCH ₂ CHOHCCl ₃ -2 (67)	1090
		„	„ „	8-CH ₃ OC ₈ H ₆ NCH ₂ CHOHCCl ₃ -2 (79)	1090
		„	„ „	8-C ₂ H ₅ OC ₈ H ₆ NCH ₂ CHOHCCl ₃ -2 (85)	1090
		„	„ „	8- <i>n</i> -C ₃ H ₇ OC ₈ H ₆ NCH ₂ CHOHCCl ₃ -2 (69)	1090
		„	„ „	8-(C ₈ H ₁₇) ₂ NCH ₂ CH ₂ OC ₈ H ₆ NCH ₂ CHOHCCl ₃ -2 (52)	1090

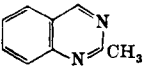
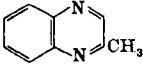
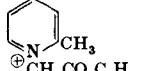
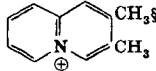
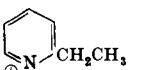
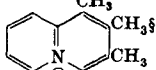
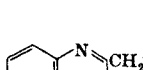
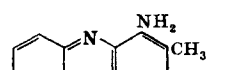
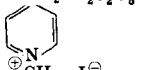
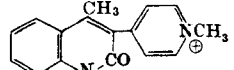
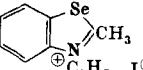
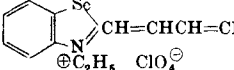
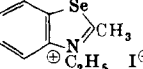
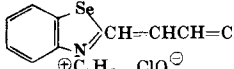
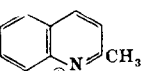
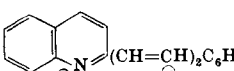
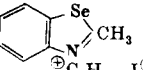
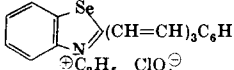
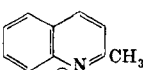
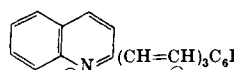
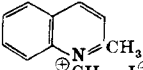
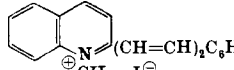
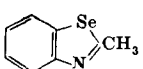
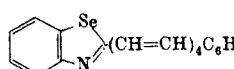
Note: References 285 to 1153 are on pp. 582–599.

ORGANIC REACTIONS

THE KNOEVENAGEL CONDENSATION

535

TABLE XVII—Continued
CONDENSATIONS WITH ACTIVE METHYLENE GROUPS ATTACHED TO HETEROCYCLIC SYSTEMS

A. Acyclic Aldehydes or Ketones—Continued					
Aldehyde or Ketone	Heterocyclic Compound	Catalyst	Temperature	Product(s) and Yield(s) (%)	Refs.
Chloral (<i>contd.</i>)		Pyridine	Water bath	2-C ₆ H ₅ N ₂ CH ₂ CHOHCCl ₃ (99)	234
		"	" "	2-C ₆ H ₅ N ₂ CH ₂ CHOHCCl ₃ (70)	234
Biacetyl	 CH ₂ CO ₂ C ₂ H ₅ Br [⊖]	(n-C ₄ H ₉) ₂ NH	Boiling C ₂ H ₅ OH	 Br [⊖] (70)	1091, 1092
	 CH ₂ CO ₂ C ₂ H ₅ Br [⊖]	"	"	 Br [⊖] (61)	1091
	 2Br [⊖]	(n-C ₄ H ₉) ₂ NH/ C ₂ H ₅ OH	0°	 Br [⊖] (60)	1093
B. Aromatic Aldehydes or Ketones					
2-Aminoaceto- phenone	 CH ₂ CO ₂ C ₂ H ₅ I [⊖]	Piperidine	Boiling C ₂ H ₅ OH	 I [⊖] (17)	68
Cinnamaldehyde	 C ₂ H ₅ I [⊖]	"	"	 C ₂ H ₅ ClO ₄ [⊖] (—)	864
4-Methoxycinna- maldehyde	 C ₂ H ₅ I [⊖]	Piperidinium acetate	"	 C ₂ H ₅ ClO ₄ [⊖] (—)	953
	 CH ₃ CH ₃ SO ₄ [⊖]	"	"	 CH ₃ ClO ₄ [⊖] (—)	953
5-Phenylpentadienal	 C ₂ H ₅ I [⊖]	Piperidine	"	 C ₂ H ₅ ClO ₄ [⊖] (—)	864
	 CH ₃ CH ₃ SO ₄ [⊖]	"	"	 CH ₃ ClO ₄ [⊖] (—)	864
4-Dimethylamino- cinnamaldehyde	 CH ₃ I [⊖]	"	"	 CH ₃ I [⊖] (—)	1094
1-Phenyl- heptatrienal	 C ₂ H ₅ I [⊖]	"	"	 C ₂ H ₅ ClO ₄ [⊖] (—)	864

Note: References 285 to 1153 are on pp. 582–599.

§ The monohydrate was isolated.

TABLE XVII—Continued
CONDENSATIONS WITH ACTIVE METHYLENE GROUPS ATTACHED TO HETEROCYCLIC SYSTEMS

538

ORGANIC REACTIONS

THE KNOEVENAGEL CONDENSATION

539

C. Aromatic Aldehydes					
Aldehyde	Heterocyclic Compound	Catalyst	Temperature	Product(s) and Yield(s) (%)	Refs.
2-Chloro-benzaldehyde		Piperidine	Boiling CH ₃ OH	 (63)	284
3-Chloro-benzaldehyde		"	"	 (72)	284
2-Nitro-benzaldehyde		"	Boiling C ₂ H ₅ OH	 (4)	68
3-Nitro-benzaldehyde		"	Boiling CH ₃ OH	 (85)	284
4-Nitro-benzaldehyde		"	"	 (—)	1095
		"	"	 (—)	1095
		"	"	 (—)	1095
		"	Boiling C ₂ H ₅ OH	 (13)	68
		"	"	 (—)	893
Benzaldehyde		None	125°	2-C ₆ H ₄ NCH=CHC ₆ H ₅ (—)	1096
		Piperidine	Boiling CH ₃ OH	 (73)	225, 284, 1095
		"	Boiling sec- C ₂ H ₅ OH	 (45)	225
		"	Boiling CH ₃ OH	 (80-85)	225, 1095

Note: References 285 to 1153 are on pp. 582-599.

TABLE XVII—Continued
CONDENSATIONS WITH ACTIVE METHYLENE GROUPS ATTACHED TO HETEROCYCLIC SYSTEMS

540

ORGANIC REACTIONS

THE KNOEVENAGEL CONDENSATION

541

C. Aromatic Aldehydes—Continued					
Aldehyde	Heterocyclic Compound	Catalyst	Temperature	Product(s) and Yield(s) (%)	Refs.
Benzaldehyde (<i>cond.</i>)		Piperidinium acetate	Boiling CH ₃ OH	(28)	225
		Piperidine	"	(—)	1095
		"	Boiling C ₂ H ₅ OH	2-C ₂ H ₅ NC(CO ₂ C ₂ H ₅)=CHC ₆ H ₅ (46) (<i>trans</i> cinnamate)	68
		"	"	(35) (<i>cis</i> cinnamate)	68
		"	"	(42)	68
		"	"	(82)	1097
Salicylaldehyde		"	"	(—)	864
		"	175°	(86)	1098
		"	175–180°	(80)	1098
		"	160°	(—)	1098
		"	160–165°	(Quant.)	1098
		"	150°	(45)	230
		"	Boiling CH ₃ OH	(82)	284

Note: References 285 to 1153 are on pp. 582–599.

|| Some monobenzylidene derivative was obtained.

¶ The product was isolated as a sodium salt.

TABLE XVII—Continued
CONDENSATIONS WITH ACTIVE METHYLENE GROUPS ATTACHED TO HETEROCYCLIC SYSTEMS

542

ORGANIC REACTIONS

THE KNOEVENAGEL CONDENSATION

543

C. Aromatic Aldehydes—Continued					
Aldehyde	Heterocyclic Compound	Catalyst	Temperature	Product(s) and Yield(s) (%)	Refs.
Salicylaldehyde (<i>contd.</i>)		Piperidine	Boiling <i>i</i> -C ₃ H ₇ OH	(—)	1099
		"	Boiling C ₂ H ₅ OH	C ₆ H ₅ N·2 (75)	68
		"	"	C ₆ H ₅ N·4 (94)	68
		"	Boiling <i>i</i> -C ₃ H ₇ OH	(—)	1099
		"	"	(—)	1099
3-Hydroxy- benzaldehyde		"	Boiling CH ₃ OH	(92)	284
4-Hydroxy- benzaldehyde		"	"	(70)	284
		"	Boiling C ₂ H ₅ OH	(70-80)	1097
		"	"	(70)	1100
3,4-Dihydroxy- benzaldehyde (protocatechuic aldehyde)		"	Boiling CH ₃ OH	(40)	284
		"	Boiling C ₂ H ₅ OH	(95)	1101
2-Amino- benzaldehyde		"	Boiling C ₂ H ₅ OH	(30)	68
4-Amino- benzaldehyde		"	Boiling <i>i</i> -C ₃ H ₇ OH	(60)	1100

Note: References 285 to 1153 are on pp. 582-599.

TABLE XVII—Continued
CONDENSATIONS WITH ACTIVE METHYLENE GROUPS ATTACHED TO HETEROCYCLIC SYSTEMS

544

ORGANIC REACTIONS

THE KNOEVENAGEL CONDENSATION

545

C. Aromatic Aldehydes—Continued					
Aldehyde	Heterocyclic Compound	Catalyst	Temperature	Product(s) and Yield(s) (%)	Refs.
3,4-Methylene-dioxybenzaldehyde (piperonal)		Piperidine	Boiling CH ₃ OH	(70)	284
4-Methylbenzaldehyde		"	"	(65)	284, 1095
		"	"	(—)	1095
		"	"	(—)	1095
4-Methoxybenzaldehyde (anisaldehyde)		"	"	(92)	284, 1095
		"	"	(—)	1095
		"	"	(—)	1095
		"	"	(—)	953
		"	Boiling C ₂ H ₅ OH	(—)	953
		"	"	(—)	187
3-Methoxy-4-hydroxybenzaldehyde (vanillin)		"	Boiling CH ₃ OH	(83)	284
		"	Boiling i-C ₃ H ₇ OH	(—)	1099
		"	Boiling C ₂ H ₅ OH	(88)	1101

Note: References 285 to 1153 are on pp. 582-599.

TABLE XVII—Continued
CONDENSATIONS WITH ACTIVE METHYLENE GROUPS ATTACHED TO HETEROCYCLIC SYSTEMS

C. Aromatic Aldehydes—Continued					
Aldehyde	Heterocyclic Compound	Catalyst	Temperature	Product(s) and Yield(s) (%)	Refs.
3-Methoxy-4-hydroxybenzaldehyde (vanillin) (contd.)		"	Boiling $i\text{-C}_3\text{H}_7\text{OH}$	 (—) 1099	
		"	"	 (—) 1099	
		Pyridine	B.p.	 (41) 1102	
		Piperidine	Boiling $\text{C}_6\text{H}_5\text{OH}$	 (64) 1102	
		"	"	 (—) 1102	
		Pyridine	B.p.	 (66) 1102	
4-Acetamidobenzaldehyde		Piperidine	Boiling $i\text{-C}_3\text{H}_7\text{OH}$	 (60) 1102	
		"	Boiling alcohol	 (43) 1100	
		"	Boiling $i\text{-C}_6\text{H}_7\text{OH}$	 (30) 1102	
		"	Boiling alcohol	 (50) 1100	
2,5-Dimethoxybenzaldehyde		"	Boiling CH_3OH	 (88) 284	

Note: References 285 to 1153 are on pp. 582-599.

TABLE XVII—Continued
CONDENSATIONS WITH ACTIVE METHYLENE GROUPS ATTACHED TO HETEROCYCLIC SYSTEMS

548

ORGANIC REACTIONS

C. Aromatic Aldehydes—Continued					
Aldehyde	Heterocyclic Compound	Catalyst	Temperature	Product(s) and Yield(s) (%)	Refs.
3,4-Dimethoxybenzaldehyde (veratraldehyde)		Piperidine	Boiling $i\text{-C}_3\text{H}_7\text{OH}$	 (88)	284
2-Hydroxy-3-ethoxybenzaldehyde		"	"	 (83)	284
4-Hydroxy-3-ethoxybenzaldehyde		"	"	 (88)	284
3-Bromo-4-dimethylamino-benzaldehyde		"	"	 (73)	284
2-Dimethylamino-benzaldehyde		"	"	 (50)	1094
3-Dimethylamino-benzaldehyde		"	Boiling $\text{C}_2\text{H}_5\text{OH}$	 (52)	1147
		"	"	 (15)	1147
		"	"	 (—)	1147
4-Dimethylamino-benzaldehyde		"	"	 (—)	893
		Piperidinium acetate	Boiling $\text{C}_4\text{H}_9\text{CH}_3$	 (12)	236
		"	"	 (18)	236
		Piperidine	Boiling CH_3OH	 (97)	284, 1095 1103
		"	"	 (—)	1095
		"	"	 (—)	1095

Note: References 285 to 1153 are on pp. 582–599.

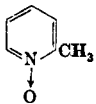
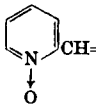
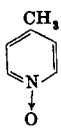
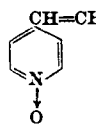

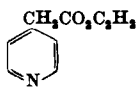
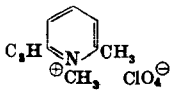
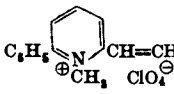
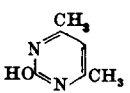
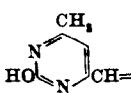
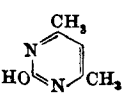
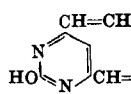


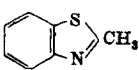

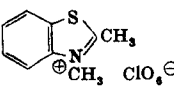
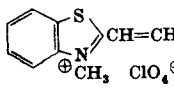
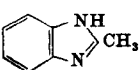

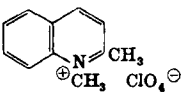
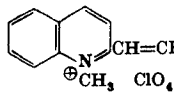
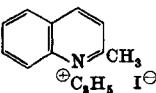
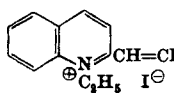
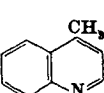

THE KNOEVENAGEL CONDENSATION

549

TABLE XVII—Continued
CONDENSATIONS WITH ACTIVE METHYLENE GROUPS ATTACHED TO HETEROCYCLIC SYSTEMS

550

ORGANIC REACTIONS

C. Aromatic Aldehydes—Continued					
Aldehyde	Heterocyclic Compound	Catalyst	Temperature	Product(s) and Yield(s) (%)	Refs.
4-Dimethyl-aminobenzaldehyde (contd.)		Piperidinium acetate	Boiling $C_6H_5CH_3$	 (13)	236
		"	"	 (12)	236
		Piperidine	Boiling C_6H_5OH	$2-C_6H_4NC(CO_2C_2H_5)=CHC_6H_4N(CH_3)_2$ (76)	68
		"	"	$4-C_6H_4NC(CO_2C_2H_5)=CHC_6H_4N(CH_3)_2$ (89)	68
		"	"	 (25)	1094
		"	"	 (55)	1101
		"	"	 (—)	1072
		Piperidinium acetate	Boiling $C_6H_5CH_3$	 (10)	222
		"	"	 (51)	222
		Piperidine	Boiling C_6H_5OH	 (60)	1094
		Piperidinium acetate	Boiling $C_6H_5CH_3$	 (50)	222
		Piperidine	Boiling C_6H_5OH	 (—)	1094
		"	"	 (—)	1094
		Piperidinium acetate	Boiling $C_6H_5CH_3$	 (23)	222

Note: References 285 to 1153 are on pp. 582-599.

THE KNOEVENAGEL CONDENSATION

551

TABLE XVII—Continued
CONDENSATIONS WITH ACTIVE METHYLENE GROUPS ATTACHED TO HETEROCYCLIC SYSTEMS

552

ORGANIC REACTIONS

THE KNOEVENAGEL CONDENSATION

553

C. Aromatic Aldehydes—Continued					
Aldehyde	Heterocyclic Compound	Catalyst	Temperature	Product(s) and Yield(s) (%)	Refs.
4-Dimethylaminobenzaldehyde (contd.)		Piperidinium acetate	Boiling $C_6H_5CH_3$	(66)	236
		"	"	(25)	1104
		Piperidine	Boiling C_2H_5OH	(—)	1094
		Piperidinium acetate	Boiling $C_6H_5CH_3$	(60)	222
		Piperidine	Boiling C_2H_5OH	(70)	1105
		Pyridine	Heat	(78)	1106
Azulene-1-carboxaldehyde		Piperidine	Boiling C_2H_5OH	(68)	1105
		"	Boiling $i-C_3H_7OH$	(50)	1100
		"	Room	(—)	1107
		"	"	(—)	1107
		"	"	(—)	1107
Azulene-1,3-dicarboxaldehyde		Piperidine/alcohol	"	(Almost quant.)	1107
		Piperidine	"	(—)	1107

Note: References 285 to 1153 are on pp. 582-599.

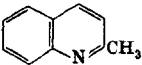
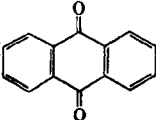

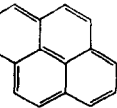
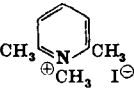
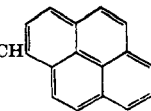
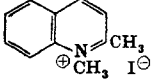
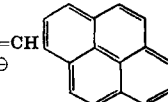

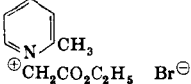
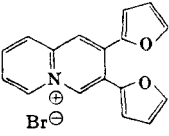
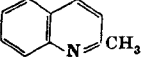
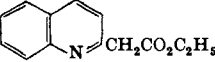
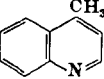
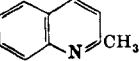
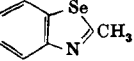
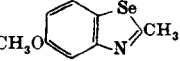
TABLE XVII—Continued
CONDENSATIONS WITH ACTIVE METHYLENE GROUPS ATTACHED TO HETEROCYCLIC SYSTEMS

C. Aromatic Aldehydes—Continued					
Aldehyde	Heterocyclic Compound	Catalyst	Temperature	Product(s) and Yield(s) (%)	Refs.
4-Methyl-(2'-chloroethyl)-aminobenzaldehyde		Piperidine	Boiling C ₂ H ₅ OH	 CH=CHC ₆ H ₄ N(CH ₃)CH ₂ CH ₂ Cl-4 (—)	898
4-Dimethylamino-benzaldehyde methiodide		"	Boiling CH ₃ OH	 CH=CHC ₆ H ₄ N(CH ₃) ₂ -4 (67) 2I [⊖]	284
2-Hydroxy-1-naphth-aldehyde		"	Boiling i-C ₃ H ₇ OH	 CH=CHC ₆ H ₄ N(CH ₃) ₂ -4 I [⊖] (—)	1099
		"	"	 CH=CHC ₆ H ₄ N(CH ₃) ₂ -4 CH ₃ SO ₄ [⊖] (—)	1099
		"	"	 CH=CHC ₆ H ₄ N(CH ₃) ₂ -4 CH ₃ SO ₄ [⊖] (—)	1099
Ferrocene-carboxaldehyde		"	Boiling CH ₃ OH	 CH=CHC ₆ H ₄ N(CH ₃) ₂ -4 I [⊖] (—)	511
4-Ethyl-(2'-chloro-ethyl)amino-benzaldehyde		"	Boiling C ₂ H ₅ OH	 CH=CHC ₆ H ₄ N(CH ₃)CH ₂ CH ₂ Cl-4 (55)	898
3-Diethylamino-benzaldehyde		"	"	 CH=CHC ₆ H ₄ N(CH ₃) ₂ -3 (—)	1147
4-Diethylamino-benzaldehyde		"	Boiling CH ₃ OH	 CH=CHC ₆ H ₄ N(CH ₃) ₂ -4 (95)	284
9,10-Phenanthra-quinone		(n-C ₄ H ₉) ₂ NH	50°	 CH=CHC ₆ H ₄ N(CH ₃) ₂ -4 Br [⊖] (40)	1091
Anthraquinone-2-carboxaldehyde		Piperidine	140–150°	 CH=CHC ₆ H ₄ N(CH ₃) ₂ -4 (10)	721

Note: References 285 to 1153 are on pp. 582–599.

** The bromide hemihydrate was isolated.

TABLE XVII—Continued
CONDENSATIONS WITH ACTIVE METHYLENE GROUPS ATTACHED TO HETEROCYCLIC SYSTEMS

C. Aromatic Aldehydes—Continued					
Aldehyde	Heterocyclic Compound	Catalyst	Temperature	Product(s) and Yield(s) (%)	Refs.
Anthraquinone-2-carboxaldehyde (contd.)		Piperidine	Boiling $C_6H_5NO_2$	$2-C_6H_5NCH=CH-$  (50)	721
Pyrene-3-carboxaldehyde		Piperidine/ C_2H_5OH	180°	$CH=CH-$  (65)	1108
		Piperidine	180°	$CH=CH-$  (70)	1108
		"	180°	$CH=CH-$  (75)	1108
D. Heterocyclic Aldehydes or Ketones					
Aldehyde or Ketone					
Pyridine-3-carboxaldehyde		Piperidine	Boiling alcohol	$CH=CHC_6H_4N-3$ (60)	1109
Furil		$(n-C_4H_9)_2NH$	Boiling C_2H_5OH	 (80)	1091
Quinoline-2-carboxaldehyde		$(C_2H_5)_2NH$	Boiling aqueous C_2H_5OH	$2-C_6H_5NCH_2CHOHC_6H_5N-2$ (75)	1110
		Piperidine	Boiling C_2H_5OH	$2-C_6H_5NCH(CO_2C_2H_5)=CHC_6H_5N-2$ (54)	1111
		$(C_2H_5)_2NH$	Boiling aqueous C_2H_5OH	$4-C_6H_5NCH_2CHOHC_6H_5N-2$ (73)	1110
Quinoline-4-carboxaldehyde		"	Boiling $n-C_3H_7OH$	$2-C_6H_5NCH_2CHOHC_6H_5N-4$ (72)	1110
Quinoline-6-carboxaldehyde		—	270°	$CH=CHC_6H_5N-6$ (29)	1112
		—	265°	$CH=CHC_6H_5N-6$ (33)	1112

Note: References 285 to 1153 are on pp. 582–599.

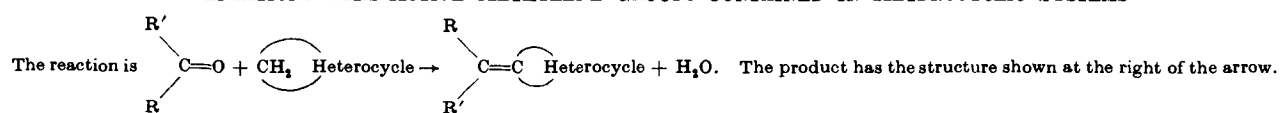
TABLE XVII—Continued
CONDENSATIONS WITH ACTIVE METHYLENE GROUPS ATTACHED TO HETEROCYCLIC SYSTEMS

D. Heterocyclic Aldehydes—Continued					
Aldehyde or Ketone	Heterocyclic Compound	Catalyst	Temperature	Product(s) and Yield(s) (%)	Refs.
Quinoline-6-carboxaldehyde (<i>contd.</i>)		—	230°	(36)	1112
3-Methylindole-2-carboxaldehyde		Piperidine	Boiling CH ₃ OH	(79)	1148
		"	"	(72)	1148

Note: References 285 to 1153 are on pp. 582-599.

TABLE XVIII

CONDENSATIONS WITH ACTIVE METHYLENE GROUPS CONTAINED IN HETEROCYCLIC SYSTEMS



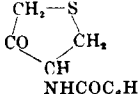





A. Acyclic Aldehydes and Ketones					
Aldehyde or Ketone	Heterocyclic Compound	Catalyst	Temperature	Yield (%)	Refs.
Acetone		Piperidinium acetate	Boiling C ₆ H ₆	(80)	1113
CH ₃ COC ₃ H ₇		"	"	(19)	1113
CH ₃ COC ₃ H _{7-n}		"	"	(23)	1113
		Piperidine + pyridine	B.p.	(87)	1114

Note: References 285 to 1153 are on pp. 582-599.

TABLE XVIII—Continued

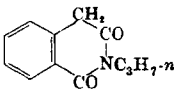
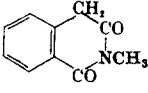
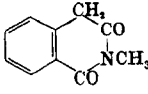
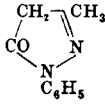
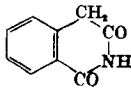
CONDENSATIONS WITH ACTIVE METHYLENE GROUPS CONTAINED IN HETEROCYCLIC SYSTEMS

A. Acyclic Aldehydes and Ketones—Continued					
Aldehyde or Ketone	Heterocyclic Compound	Catalyst	Temperature	Yield (%)	Refs.
1-Hexen-5-one		Piperidinium acetate	Boiling C ₆ H ₆	(65)	1113
CH ₃ COC ₄ H _{9-n}		"	"	(36)	1113
		Piperidine + pyridine	B.p.	(72)	1114
CH ₃ COC ₄ H _{9-i}		Piperidinium acetate	Boiling C ₆ H ₆	(16)	1113
C ₂ H ₅ COC ₃ H _{7-n}		Piperidine + pyridine	B.p.	(50)	1114

Ethyl 4-formylbutyrate		Piperidine + CH ₃ CO ₂ H	—	(50)	1115
CH ₃ COC ₆ H ₁₁ -n		Piperidinium acetate	Boiling C ₆ H ₆	(43)	1113
(n-C ₃ H ₇) ₂ CO		Piperidine + pyridine	B.p.	(35)	1114
CH ₃ COC ₆ H ₁₃ -n		Piperidinium acetate	Boiling C ₆ H ₆	(27)	1113
n-C ₃ H ₇ COC ₆ H ₉ -n		Piperidine + pyridine	B.p.	(28)	1114
(n-C ₄ H ₉) ₂ CO		„	B.p.	(25)	1114

Note: References 285 to 1153 are on pp. 582-599.

TABLE XVIII—Continued
CONDENSATIONS WITH ACTIVE METHYLENE GROUPS CONTAINED IN HETEROCYCLIC SYSTEMS

B. Alkyl Aldehydes					
Aldehyde	Heterocyclic Compound	Catalyst	Temperature	Yield (%)	Refs.
Cinnamaldehyde		—	Boiling C ₂ H ₅ OH	(—)	1116
Phenylglyoxal		Piperidine	„	(85)	1117
3,4-Methylenedioxyphenyl-acetaldehyde		Piperidine/alcohol	Warm	(80)	238
4-Dimethylaminocinnam-aldehyde		Piperidinium acetate	Boiling C ₂ H ₅ OH	(—)	760
C. Aromatic Aldehydes					
2-Nitrobenzaldehyde		Piperidine + pyridine	Boil, then water bath	(80)	1118

		"	"	(—)	1118
		"	"	(—)	1118
4-Nitrobenzaldehyde		(C ₂ H ₅) ₃ N	Boiling aqueous C ₂ H ₅ OH	(97)	1119
Benzaldehyde		Piperidine	Boiling C ₂ H ₅ OH	(*)	1120
		Morpholine/pyridine	B.p.	(92)	1121
		Piperidine + pyridine	„	(33)	1122
		(C ₂ H ₅) ₂ NH + pyridine	100°	(76)	1122

Note: References 285 to 1153 are on pp. 582-599.

* The *bis* condensation product $\text{Het} \text{---} \text{CHCH}(\text{C}_6\text{H}_5) \text{---} \text{CH} \text{---} \text{Het}$ was obtained.

TABLE XVIII—Continued
CONDENSATIONS WITH ACTIVE METHYLENE GROUPS CONTAINED IN HETEROCYCLIC SYSTEMS

C. Aromatic Aldehydes—Continued					
Aldehyde	Heterocyclic Compound	Catalyst	Temperature	Yield (%)	Refs.
Benzaldehyde (<i>contd.</i>)		Piperidine + pyridine	B.p.	(92)	1122
		(C ₂ H ₅) ₂ NH, piperidine, or piperidinium acetate	—	(—)	1115
		Piperidine/CH ₃ OH	—	(29)	1115
		—	Boiling C ₂ H ₅ OH	(—)	1116
4-Hydroxybenzaldehyde		Piperidine or (C ₂ H ₅) ₂ NH + pyridine	100°	(15, 65)	1122
		Morpholine/glycerol	160°	(80)	1123

		Piperidine + pyridine	B.p.	(95-100)	1122
3,4-Methylenedioxybenzaldehyde (piperonal)			Boiling C ₄ H ₉ OH	(—)	1116
4-Methoxybenzaldehyde (anisaldehyde)		Piperidine or (C ₄ H ₉) ₃ NH + pyridine	B.p., or 100°	(14, 94)	1122
		Piperidine + pyridine	B.p.	(95)	1122
3,4-Dimethoxybenzaldehyde (veratraldehyde)		Piperidinium acetate	Boiling C ₄ H ₉ CH ₃	(80)	241
4-Dimethylaminobenzaldehyde		"	Boiling C ₄ H ₉ OH	(—)	894
		"	"	(—)	894

Note: References 285 to 1153 are on pp. 582-599.

† The group R was C₆H₅, n-C₄H₉, or allyl.

TABLE XVIII—Continued
CONDENSATIONS WITH ACTIVE METHYLENE GROUPS CONTAINED IN HETEROCYCLIC SYSTEMS

C. Aromatic Aldehydes—Continued					
Aldehyde	Heterocyclic Compound	Catalyst	Temperature	Yield (%)	Refs.
CH ₃ N[CHO]		Piperidine	Boiling i-C ₄ H ₉ OH	(95)†	909
4-Methyl(isooctyl)amino- benzaldehyde		"	Boiling alcohol	(—)	240
N[CHO]		"	Boiling i-C ₄ H ₉ OH	(96)§	909
D. Heterocyclic Aldehydes					
5-Nitrothiophene-2- carboxaldehyde		Piperidine	—	(—)	581
Furfural		—	Boiling C ₄ H ₉ OH	(—)	1116
Pyrrole-2-carboxaldehyde		Piperidine	"	(73)	239

Pyridine-2-carboxaldehyde		(C ₂ H ₅) ₂ NH	80°	(55)	911
Indole-3-carboxaldehyde		Piperidine	B.p.	(65)	1124
		"	B.p.	(Quant.)	1125
		"	200°	(75)	237
		"	200°	(—)	237
		Piperidinium acetate	20°	(90)	242
1-Methylindole-3-carboxaldehyde		Piperidine	200°	(90)	237

Note: References 285 to 1153 are on pp. 582-599.

‡ The *bis* condensation product was obtained.

§ The *tris* condensation product was obtained.

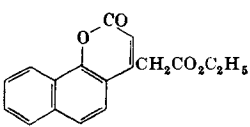
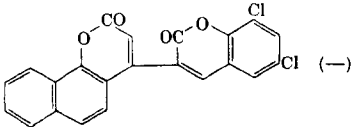
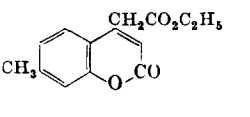
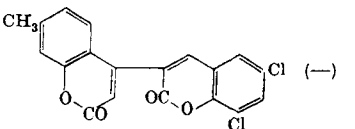
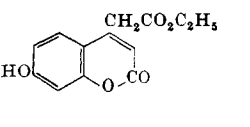
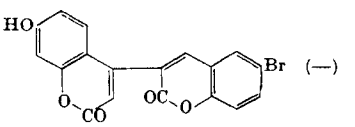
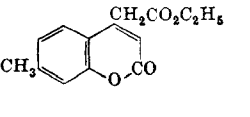
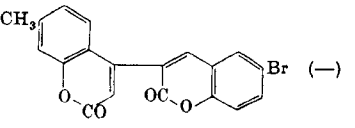
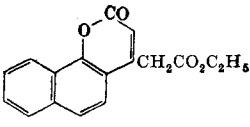
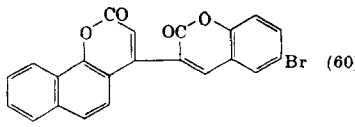
|| R was C₂H₅, n-C₄H₉, or allyl.

TABLE XVIII—Continued
CONDENSATIONS WITH ACTIVE METHYLENE GROUPS CONTAINED IN HETEROCYCLIC SYSTEMS

D. Heterocyclic Aldehydes—Continued					
Aldehyde	Heterocyclic Compound	Catalyst	Temperature	Yield (%)	Refs.
1-Methylindole-3-carboxaldehyde (contd.)		Piperidine	200°	(90)	237
5-Methoxyindole-3-carboxaldehyde		"	B.p.	(95)	1126
6-Methoxyindole-3-carboxaldehyde		"	B.p.	(72)	1127
7-Methoxyindole-3-carboxaldehyde		"	B.p.	(71)	1126
		Piperidinium acetate	20°	(89)	242
		"	20°	(87)	242

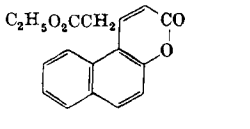
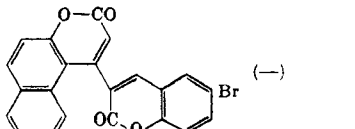
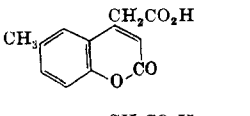
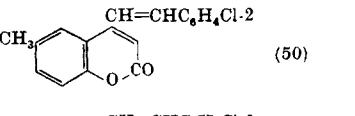
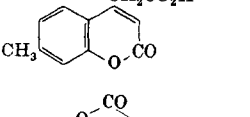
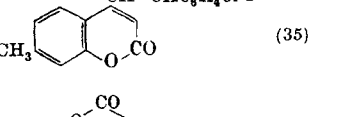
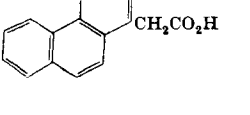
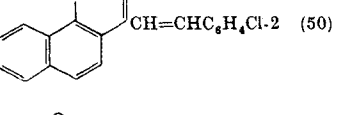
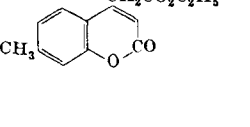
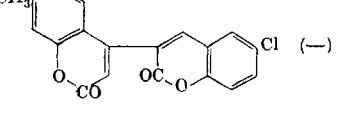
Note: References 285 to 1153 are on pp. 582-599.

TABLE XIX
CONDENSATIONS WITH ARYLACETIC ACIDS AND THEIR DERIVATIVES

A. Aromatic Aldehydes					
Aldehyde	Arylacetic Acid or Derivative	Catalyst	Temperature	Product(s) and Yield(s) (%)	Refs.
3,5-Dichloro-2-hydroxy-benzaldehyde		Piperidine	Boiling C ₂ H ₅ OH	 (—)	1128
		"	"	 (—)	1128
5-Bromo-2-hydroxy-benzaldehyde		"	"	 (—)	1128
		"	"	 (—)	1128
		"	"	 (60)	1128

Note: References 285 to 1153 are on pp. 582-599.

TABLE XIX—Continued
CONDENSATIONS WITH ARYLACETIC ACIDS AND THEIR DERIVATIVES

A. Aromatic Aldehydes—Continued					
Aldehyde	Arylacetic Acid or Derivative	Catalyst	Temperature	Product(s) and Yield(s) (%)	Refs.
5-Bromo-2-hydroxy-benzaldehyde (<i>contd.</i>)		Piperidine	Boiling C ₂ H ₅ OH	 (—)	1128
2-Chlorobenzaldehyde		Piperidine + pyridine	125-130°	 (50)	244
		"	125-130°	 (35)	244
		"	125-130°	 (50)	244
5-Chloro-2-hydroxy-benzaldehyde		Piperidine	Boiling C ₂ H ₅ OH	 (—)	1128

		"	"		1128
		"	"		1128
5-Nitro-2-hydroxy-benzaldehyde		"	"		1128
Benzaldehyde	$C_6H_5CH_2CO_2C_2H_5$	"	B.p.	$C_6H_5CH=C(CO_2C_2H_5)C_6H_5$ (10)	690
		"	Boiling C_2H_5OH		1129
		Piperidine + pyridine	125-130°		1130
		"	125-130°		244

Note: References 285 to 1153 are on pp. 582-599.

TABLE XIX—Continued
CONDENSATIONS WITH ARYLACETIC ACIDS AND THEIR DERIVATIVES

A. Aromatic Aldehydes—Continued					
Aldehyde	Arylacetic Acid or Derivative	Catalyst	Temperature	Product(s) and Yield(s) (%)	Refs.
Benzaldehyde (contd.)		Piperidine + pyridine	125-130°		1130
2-Hydroxy-benzaldehyde		Piperidine	Boiling C_2H_5OH		1128
		"	"		1128
		"	"		1128
		Piperidine + pyridine	"		1129

		Piperidine	..		1131
4-Hydroxy-benzaldehyde	$C_6H_5CH_2CO_2H$..	110°	$C_6H_5CH=CHC_6H_4OH-4$ (-)	1132
3,4-Methylenedioxy-benzaldehyde (piperonal)	$C_6H_5CH_2CO_2H$..	170°	$C_6H_5CH=CHC_6H_3O_2CH_2-3,4$ (-) $C_6H_5C(CO_2H)=CHC_6H_3O_2CH_2-3,4$ (-)	243
		Piperidine + pyridine	125-130°	$CH=CHC_6H_3O_2CH_2-3,4$ (45)	1130
		$CH=CHC_6H_3O_2CH_2-3,4$ (20)	244
		$CH=CHC_6H_3O_2CH_2-3,4$ (45)	1130
4-Methylbenzaldehyde		$CH=CHC_6H_4CH_3-4$ (45)	1130

Note: References 285 to 1153 are on pp. 582-599.

* Compounds in which R was Cl, Br, or I were used.

TABLE XIX—Continued
CONDENSATIONS WITH ARYLACETIC ACIDS AND THEIR DERIVATIVES

A. Aromatic Aldehydes—Continued					
Aldehyde	Arylacetic Acid or Derivative	Catalyst	Temperature	Product(s) and Yield(s) (%)	Refs.
4-Methylbenzaldehyde (contd.)		Piperidine + pyridine	125-130°	$CH=CHC_6H_4CH_3-4$ (45)	1130
2-Methoxy-benzaldehyde	$C_6H_5CH_2CO_2H$	Piperidine	160°	$C_6H_5C(CO_2H)=CC_6H_4OCH_3-2$ (-)	1132
		Piperidine + pyridine	125-130°	$CH=CHC_6H_4OCH_3-2$ (60)	244
		$CH=CHC_6H_4OCH_3-2$ (60)	244
		$CH=CHC_6H_4OCH_3-2$ (65)	244
4-Methoxy-benzaldehyde (anisaldehyde)	CH_3CO_2H	Piperidine	130-135°	$CH=CHC_6H_4OCH_3-4$ (-)	243
		Piperidine + pyridine	125-130°	$CH=CHC_6H_4OCH_3-4$ (45)	244

		Piperidine	130-135°		243
3-Methoxy-4-hydroxy- benzaldehyde (vanillin)	$C_6H_5CH_2CO_2H$	"	140-150°	$C_6H_5CH=CHC_6H_4OH \cdot 4 \cdot OCH_3 \cdot 3$ (—)	243
		"	140°	$CH=CHC_6H_4OH \cdot 4 \cdot OCH_3 \cdot 3$ (—)	243
		Piperidine + pyridine	125-130°	$CH=CHC_6H_4OH \cdot 4 \cdot OCH_3 \cdot 3$ (30)	244
		"	"	$CH=CHC_6H_4OH \cdot 4 \cdot OCH_3 \cdot 3$ (65)	1130
4-Dimethylamino- benzaldehyde	$C_6H_5CH_2CO_2H$	Piperidine	160°	$C_6H_5CH=CHC_6H_4N(CH_3)_2 \cdot 4$ (—)	243
		"	140-150°	$CH=CHC_6H_4N(CH_3)_2 \cdot 4$ (—)	243
		"	140°	$CH=CHC_6H_4N(CH_3)_2 \cdot 4$ (—)	243

Note: References 285 to 1153 are on pp. 582-599.

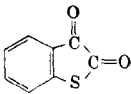
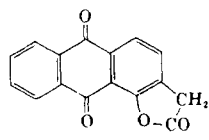
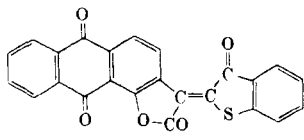
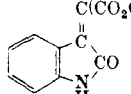
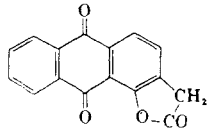
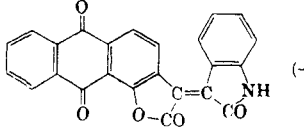
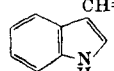
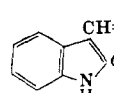
TABLE XIX—Continued
CONDENSATIONS WITH ARYLACETIC ACIDS AND THEIR DERIVATIVES

A. Aromatic Aldehydes—Continued

Aldehyde	Arylacetic Acid or Derivative	Catalyst	Temperature	Product(s) and Yield(s) (%)	Refs.
4-Dimethylamino- benzaldehyde (contd.)		Piperidinium acetate	Boiling CH_3CO_2H		(—) 1129
2-Hydroxy-1- naphthaldehyde		Piperidine	Boiling $(C_2H_5)_2O$		(—) 1128
		Piperidinium acetate	Boiling CH_3CO_2H		1129
		"	"		1129

B. Heterocyclic Aldehydes and Ketones

Aldehyde or Ketone

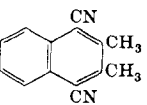



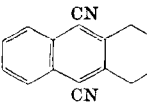
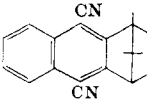
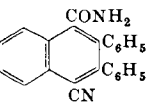
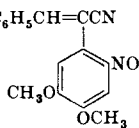
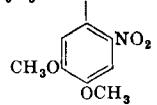
		Piperidine + pyridine	Boiling C_2H_5OH	 (—)	1129
Isatin	$C_6H_5CH_2CO_2C_2H_5$	$(C_2H_5)_2NH$	„	$C(CO_2C_2H_5)_2C_6H_5$  (71)	932
		Piperidine	„	 (—)	1129
Indole-3-carboxaldehyde	$C_6H_5CH_2CO_2C_2H_5$	„	200°	 $CH=C(CO_2C_2H_5)C_6H_5$ (53)	237
2-Phenylindole-3-carboxaldehyde	$C_6H_5CH_2CO_2C_2H_5$	„	B.p.	 $CH=C(CO_2C_2H_5)C_6H_5$ (52)	923

Note: References 285 to 1153 are on pp. 582-599.

TABLE XX
CONDENSATIONS WITH NITRILES (INCLUDING β -KETONIC NITRILES)

578

ORGANIC REACTIONS

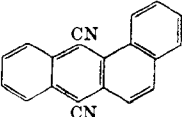
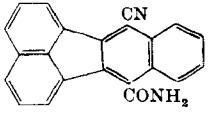
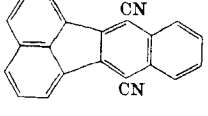
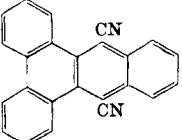
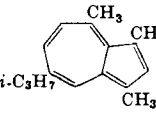

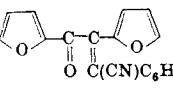
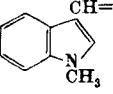
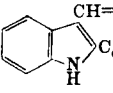
A. Acyclic Aldehydes and Ketones					
Aldehyde or Ketone	Cyanide	Catalyst	Temperature	Product(s) and Yield(s) (%)	Refs.
Glyoxal	$C_6H_5COCH_2CN$	Piperidine	Slight warming	$C_6H_5COC(CN)=CHCH=C(CN)COC_6H_5$ (—)	191
Biacetyl	$1,2-C_6H_4(CH_2CN)_2$	„	Heat, then cool	 (65)	245
B. Alicyclic Ketones					
Cyclohexanone	$C_6H_5COCH_2CN$	Dowex 3 acetate	Boiling C_6H_6	 (89)	141
	$2,4-(CH_3)_2C_6H_3COCH_2CN$	„	„	 (86)	141
	$(CH_3)_3CCOCH_2CN$	„	„	 (89)	141
Cyclohexane-1,2-dione	$1,2-C_6H_4(CH_2CN)_2$	Piperidine	Room	 (54)	245
Camphane-2,3-dione	„	„	„	 (90)	245
C. Aromatic Aldehydes and Ketones					
4-Dimethylamino-cinnamaldehyde	$C_6H_5COCH_2CN$	Piperidinium acetate	Boiling C_2H_5OH	$4-(CH_3)_2NC_6H_4CH=CHCH=C(CN)COC_6H_5$ (—)	760
Benzil	$1,2-C_6H_4(CH_2CN)_2$	50% aqueous piperidine	Room	 (—)	245
D. Aromatic Aldehydes and Ketones					
4-Nitrobenzaldehyde	$C_6H_5COCH_2CN$	Piperidine	Slight warming	$4-O_2NC_6H_4CH=C(CN)COC_6H_5$ (—)	191
	$C_6H_5COCH_2CN$	„	„	$C_6H_5CH=C(CN)COC_6H_5$ (82)	191
2-Nitro-4,5-dimethylbenzyl cyanide	2-Nitro-4,5-dimethylbenzyl cyanide	Piperidine, boiling abs. C_2H_5OH	„	 (90)	1153
				$C_6H_5CH=CCN$	
Terephthalaldehyde	$C_6H_5COCH_2CN$	„	Room	$1,4-[C_6H_5COC(CN)=CH]_2C_6H_4$ (82)	191
3,4-Methylene dioxy-benzaldehyde (piperonal)	$C_6H_5COCH_2CN$	Piperidine/alcohol	„	$3,4-CH_2O_2C_6H_3CH=C(CN)COC_6H_5$ (—)	769
4-Methoxybenzaldehyde (anisaldehyde)	$C_6H_5COCH_2CN$	Piperidine	Slight warming	$4-CH_3OC_6H_4CH=C(CN)COC_6H_5$ (Quant.)	191
4-Hydroxy-3-methoxybenzaldehyde (vanillin)	$C_6H_5COCH_2CN$	None	Boiling C_2H_5OH	$4-HO-3-CH_3OC_6H_3CH=C(CN)COC_6H_5$ (55)	769
2,4-Dimethoxybenzaldehyde	$C_6H_5COCH_2CN$	Piperidine/alcohol	Room	$2,4-(CH_3O)_2C_6H_3CH=C(CN)COC_6H_5$ (65)	769
3,4-Dimethoxybenzaldehyde (veratraldehyde)	$C_6H_5COCH_2CN$	„	„	$3,4-(CH_3O)_2C_6H_3CH=C(CN)COC_6H_5$ (—)	769
	2-Nitro-4,5-dimethoxybenzyl cyanide	Piperidine, boiling abs. C_2H_5OH	„	 (86)	1153

Note: References 285 to 1153 are on pp. 582-599.

THE KNOEVENAGEL CONDENSATION

579

TABLE XX—Continued
CONDENSATIONS WITH NITRILES (INCLUDING β -KETONIC NITRILES)

D. Aromatic Aldehydes and Ketones—Continued					
Aldehyde or Ketone	Cyanide	Catalyst	Temperature	Product(s) and Yield(s) (%)	Refs.
4-Dimethylamino-benzaldehyde	$C_6H_5COCH_2CN$	Piperidine or piperidinium acetate	Boiling C_2H_5OH or C_6H_6	$4-(CH_3)_2NC_6H_4CH=C(CN)COC_6H_5$ (—)	191, 893, 894
	4-O ₂ N-3,5-(CH ₃) ₂ C ₆ H ₂ CH ₂ CN*	Pyridine/ C_2H_5OH	80°	None	799
	2-C ₂ H ₅ O ₂ CC ₆ H ₄ CH ₂ CN	Piperidine or piperidinium acetate	Boiling C_2H_5OH or C_6H_6	$4-(CH_3)_2NC_6H_4CH=C(CN)C_6H_4CO_2C_2H_5 \cdot 2$ (—)	894
	2-C ₄ H ₉ SCOCH ₂ CN	"	"	$4-(CH_3)_2NC_6H_4CH=C(CN)COC_4H_9S \cdot 2$ (80)	762, 894
1,2-Naphthoquinone	1,2-C ₆ H ₄ (CH ₂ CN) ₂	Piperidine	Room	 (44)	245
6-Dimethylamino-fulvene-1,2-dicarboxaldehyde	$C_6H_5COCH_2CN$	"	"	$(CH_3)_2NCH=C(CH=CH-C(CN)COC_6H_5)_2$ (48)	711
4-Methyl-(2'-cyanoethyl)amino-benzaldehyde	"	Piperidinium acetate	Boiling C_6H_6	$4-CH_3(NCCH_2CH_2)NC_6H_4CH=C(CN)COC_6H_5$ (—)	894
Acenaphthene-1,2-dione	1,2-C ₆ H ₄ (CH ₂ CN) ₂	Piperidine	Room	 (63)	245
	"	"	Ice, then room	 (65)	1149
9,10-Phenanthraquinone	1,2-C ₆ H ₄ (CH ₂ CN) ₂	"	Room	 (30)	245
3,8-Dimethyl-5-isopropylazulene-1-carboxaldehyde	$C_6H_5CH_2CN$	Piperidine/ C_2H_5OH	"	 (78)	568
E. Heterocyclic Aldehydes and Ketones					
4,5-Dichlorothiophene-2-carboxaldehyde	4-O ₂ NC ₆ H ₄ CH ₂ CN	Piperidine	—	 (59)	578
Indole-3-carboxaldehyde	$C_6H_5CH_2CN$	"	200°	$3-C_6H_5NCH=C(CN)C_6H_5$ (93)	237
Furil	$C_6H_5CH_2CN$	"	Boiling C_2H_5OH	 (—)	734
1-Methylindole-3-carboxaldehyde	$C_6H_5CH_2CN$	"	200°	 (82)	237
2-Phenylindole-3-carboxaldehyde	$C_6H_5CH_2CN$	Piperidine + pyridine	B.p.	 (76)	923

Note: References 285 to 1153 are on pp. 582–599.

* A number of other phenylacetonitriles were used with piperidine or pyridine, but no condensations were achieved.⁷⁹⁹

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